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(54) Title: NOVEL MOLECULES OF THE TANGO-77 RELATED PROTEIN FAMILY AND USES THEREOF (57) Abstract <p>Novel Tango-77 polypeptides, proteins, and nucleic acid molecules are disclosed. In addition to isolated, full-length Tango-77 proteins, the invention further provides isolated Tango-77 fusion proteins, antigenic peptides and anti-Tango-77 antibodies. The invention also provides Tango-77 nucleic acid molecules, recombinant expression vectors containing a nucleic acid molecule of the invention, host cells into which the expression vectors have been introduced and non-human transgenic animals in which a Tango-77 gene has been introduced or disrupted. Diagnostic, screening and therapeutic methods utilizing compositions of the invention are also provided.</p>		

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NOVEL MOLECULES OF THE TANGO-77 RELATED PROTEIN
FAMILY AND USES THEREOF

Background of the Invention

The polypeptide cytokine interleukin-1 (IL-1) is a critical mediator of inflammatory and overall immune response. To date, three members of the IL-1 family, IL-1 α , IL-1 β and IL-1ra (Interleukin-1 receptor antagonist) have been isolated and cloned. IL-1 α and IL-1 β are proinflammatory cytokines which elicit biological responses, whereas IL-1ra is an antagonist of IL-1 α and IL-1 β activity. Two distinct cell-surface receptors have been identified for these ligands, the type I IL-1 receptor (IL-1RtI) and type II IL-1 receptor (IL-1RtII). Recent results suggest that the IL-1RtI is the receptor responsible for transducing a signal and producing biological effects.

As mentioned above, IL-1 is a key mediator of the host inflammatory response. While inflammation is an important homeostatic mechanism, aberrant inflammation has the potential for inducing damage to the host. Elevated IL-1 levels are known to be associated with a number of diseases particularly autoimmune diseases and inflammatory disorders.

Since IL-1ra is a naturally occurring inhibitor of IL-1, IL-1ra can be used to limit the aberrant and potentially deleterious effects of IL-1. In experimental animals, pretreatment with IL-1ra has been shown to prevent death resulting from lipopolysaccharide-induced sepsis. The relative absence of IL-1ra has also been suggested to play a role in human inflammatory bowel disease.

Summary of the Invention

The present invention is based, at least in part, on the discovery of a gene encoding Tango-77, a secreted

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protein that is predicted to be a member of the cytokine superfamily. The Tango-77 cDNA described below (SEQ ID NO:1) has three possible open reading frames. The first potential open reading frame encompasses 534 nucleotides
5 extending from nucleotide 356 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:3) and encodes a 178 amino acid protein (SEQ ID NO:2). This protein may include a predicted signal sequence of about 63 amino acids (from about amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID
10 NO:4) and a predicted mature protein of about 115 amino acids (from about amino acid 64 to amino acid 178 of SEQ ID NO:2 (SEQ ID NO:5)).

The second potential open reading frame encompasses 498 nucleotides extending from nucleotide 389
15 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:6) and encodes a 167 amino acid protein (SEQ ID NO:7). This protein may include a predicted signal sequence of about 52 amino acids (from about amino acid 1 to about amino acid 52 of SEQ ID NO:7 (SEQ ID NO:8)) and a predicted
20 mature protein of about 115 amino acids (from about amino acid 52 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:9)).

The third potential open reading frame encompasses 408 nucleotides extending from nucleotide 481 to nucleotide 889 of SEQ ID NO:1 (SEQ ID NO:10) and encodes
25 a 136 amino acid protein (SEQ ID NO:11). This protein includes a predicted signal sequence of about 21 amino acids (from about amino acid 1 to about amino acid 21 of SEQ ID NO:11 (SEQ ID NO:12)) and a predicted mature protein of about 115 amino acids (from about amino acid
30 22 to amino acid 136 of SEQ ID NO:11 (SEQ ID NO:13)).

As used herein, the terms "Tango-77", "Tango-77 protein", "Tango-77 polypeptide" and the like, can refer and polypeptide produced by the cDNA of SEQ ID NO:1 including any and all of the Tango-77 gene products
35 described above.

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Tango-77 is expected to inhibit inflammation and play a functional role similar to that of secreted IL-1ra. For example, it is expected that Tango-77 may bind to the IL-1 receptor, thus blocking receptor
5 activation by inhibiting the binding of IL-1 α and IL-1 β to the receptor. Alternatively, Tango-77 may inhibit inflammation through another pathway, for example, by binding to a novel receptor. Accordingly, Tango-77 may be useful as a modulating agent in regulating a variety
10 of cellular processes including acute and chronic inflammation, e.g., asthma, chronic myelogenous leukemia, rheumatoid arthritis, psoriasis and inflammatory bowel disease.

In one aspect, the invention provides isolated
15 nucleic acid molecules encoding Tango-77 or biologically active portions thereof, as well as nucleic acid fragments suitable as primers or hybridization probes for the detection of Tango-77.

The invention encompasses methods of diagnosing
20 and treating patients who are suffering from a disorder associated with an abnormal level (undesirably high or undesirably low) of inflammation, abnormal activity of the IL-1 receptor complex, or abnormal activity of IL-1, by administering a compound that modulates the expression
25 of Tango-77 (at the DNA, mRNA or protein level, e.g., by altering mRNA splicing) or by altering the activity of Tango-77. Examples of such compounds include small molecules, antisense nucleic acid molecules, ribozymes, and polypeptides.

30 The invention features a nucleic acid molecule which is at least 45% (e.g., 55%, 65%, 75%, 85%, 95%, or 98%) identical to the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the nucleotide sequence of the cDNA insert of the plasmid

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deposited with ATCC as Accession Number (the "cDNA of ATCC 98807"), or a complement thereof.

The invention features a nucleic acid molecule which includes a fragment of at least 100 (e.g., 250,
5 325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, 900, or 989) nucleotides of the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the nucleotide sequence of the cDNA ATCC 98807, or a complement thereof.

10 The invention also features a nucleic acid molecule which includes a nucleotide sequence encoding a protein having an amino acid sequence that is at least 45% (55%, 65%, 75%, 85%, 95%, or 98%) identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID
15 NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, or the amino acid sequence encoded by the cDNA of ATCC 98807.

In a preferred embodiment, a Tango-77 nucleic acid molecule has the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the
20 nucleotide sequence of the cDNA of ATCC 98807.

Also within the invention is a nucleic acid molecule which encodes a fragment of a polypeptide having the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID
25 NO:11, SEQ ID NO:12, SEQ ID NO:13, wherein the fragment includes at least 15 (e.g., 25, 30, 50, 100, 150, or 178) contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or the polypeptide
30 encoded by the cDNA of ATCC Accession Number 98807.

The invention includes a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8,
35 SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or

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an amino acid sequence encoded by the cDNA of ATCC
Accession Number 98807, wherein the nucleic acid molecule
hybridizes to a nucleic acid molecule comprising SEQ ID
NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or a
5 complement thereof under stringent conditions.

Also within the invention are: an isolated
Tango-77 protein having an amino acid sequence that is at
least about 45%, preferably 65%, 75%, 85%, 95%, or 98%
identical to the amino acid sequence of SEQ ID NO:5, SEQ
10 ID NO:9 or SEQ ID NO:13 (mature human Tango-77), or the
amino acid sequence of SEQ ID NO:2, SEQ ID NO:7 or SEQ ID
NO:11 (immature human Tango-77).

Also within the invention are: an isolated
Tango-77 protein which is encoded by a nucleic acid
15 molecule having a nucleotide sequence that is at least
about 65%, preferably 75%, 85%, or 95% identical to SEQ
ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the cDNA of ATCC
98807; and an isolated Tango-77 protein which is encoded
by a nucleic acid molecule having a nucleotide sequence
20 which hybridizes under stringent hybridization conditions
to a nucleic acid molecule having the nucleotide sequence
of SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the non-coding
strand of the cDNA of ATCC 98807, or the complement
thereof.

25 Also within the invention is a polypeptide which
is a naturally occurring allelic variant of a polypeptide
that includes the amino acid sequence of SEQ ID NO:2, SEQ
ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID
NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an
30 amino acid sequence encoded by the cDNA insert of the
plasmid deposited with ATCC as Accession Number 98807,
wherein the polypeptide is encoded by a nucleic acid
molecule which hybridizes to a nucleic acid molecule
comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID

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NO:10 or the complement thereof under stringent conditions.

Another embodiment of the invention features Tango-77 nucleic acid molecules which specifically detect
5 Tango-77 nucleic acid molecules relative to nucleic acid molecules encoding other members of the cytokine superfamily. For example, in one embodiment, a Tango-77 nucleic acid molecule hybridizes under stringent conditions to a nucleic acid molecule comprising the
10 nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement thereof. In another embodiment, the Tango-77 nucleic acid molecule is at least 300 (325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, 900, or 989)
15 nucleotides in length and hybridizes under stringent conditions to a nucleic acid molecule comprising the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement thereof. In yet another embodiment, the
20 invention provides an isolated nucleic acid molecule which is antisense to the coding strand of a Tango-77 nucleic acid.

Another aspect of the invention provides a vector, e.g., a recombinant expression vector, comprising a
25 Tango-77 nucleic acid molecule of the invention. In another embodiment, the invention provides a host cell containing such a vector. The invention also provides a method for producing Tango-77 protein by culturing, in a suitable medium, a host cell of the invention containing
30 a recombinant expression vector such that a Tango-77 protein is produced.

Another aspect of this invention features isolated or recombinant Tango-77 proteins and polypeptides. Preferred Tango-77 proteins and polypeptides possess at
35 least one biological activity possessed by naturally

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occurring human Tango-77, e.g., (i) the ability to interact with proteins in the Tango-77 signalling pathway (ii) the ability to interact with a Tango-77 ligand or receptor; or (iii) the ability to interact with an intracellular target protein, (iv) the ability to interact with a protein involved in inflammation and (v) the ability to bind the IL-1 receptor. Other activities include the induction and suppression of polypeptide interleukins, cytokines and growth factors.

10 The Tango-77 proteins of the present invention, or biologically active portions thereof, can be operably linked to a non-Tango-77 polypeptide (e.g., heterologous amino acid sequences) to form Tango-77 fusion proteins. The invention further features antibodies that
15 specifically bind Tango-77 proteins, such as monoclonal or polyclonal antibodies. In addition, the Tango-77 proteins or biologically active portions thereof can be incorporated into pharmaceutical compositions, which optionally include pharmaceutically acceptable carriers.

20 In another aspect, the present invention provides a method for detecting the presence of Tango-77 activity or expression in a biological sample by contacting the biological sample with an agent capable of detecting an indicator of Tango-77 activity or expression such that
25 the presence of Tango-77 activity or expression is detected in the biological sample.

 In another aspect, the invention provides a method for modulating Tango-77 activity comprising contacting a cell with an agent that modulates (inhibits or
30 stimulates)

Tango-77 activity or expression such that Tango-77 activity or expression in the cell is modulated. In one embodiment, the agent is an antibody that specifically binds to Tango-77 protein. In another embodiment, the

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agent modulates expression of Tango-77 by modulating transcription of a Tango-77 gene, splicing of a Tango-77 mRNA, or translation of a Tango-77 mRNA. In yet another embodiment, the agent is a nucleic acid molecule having a
5 nucleotide sequence that is antisense to the coding strand of the Tango-77 mRNA or the Tango-77 gene.

In one embodiment, the methods of the present invention are used to treat a subject having a disorder characterized by aberrant Tango-77 protein activity or
10 nucleic acid expression by administering an agent which is a Tango-77 modulator to the subject. In one embodiment, the Tango-77 modulator is a Tango-77 protein. In another embodiment, the Tango-77 modulator is a Tango-77 nucleic acid molecule. In other embodiments,
15 the Tango-77 modulator is a peptide, peptidomimetic, or other small molecule. In a preferred embodiment, the disorder characterized by aberrant Tango-77 protein or nucleic acid expression can include chronic and acute inflammation.

20 The present invention also provides a diagnostic assay for identifying the presence or absence of a genetic lesion or mutation characterized by at least one of: (i) aberrant modification or mutation of a gene encoding a Tango-77 protein; (ii) mis-regulation of a
25 gene encoding a Tango-77 protein; and (iii) aberrant post-translational modification of a Tango-77 protein, wherein a wild-type form of the gene encodes a protein with a Tango-77 activity.

In another aspect, the invention provides a
30 method for identifying a compound that binds to or modulates the activity of a Tango-77 protein. In general, such methods entail measuring a biological activity of a Tango-77 protein in the presence and absence of a test compound and identifying those

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compounds which alter the activity of the Tango-77 protein.

The invention also features methods for identifying a compound which modulates the expression of Tango-77 by measuring the expression of Tango-77 in the presence and absence of a compound.

Other features and advantages of the invention will be apparent from the following detailed description and claims.

10 Brief Description of the Drawings

Figure 1 depicts the cDNA sequence (SEQ ID NO:1) of Tango-77. The Tango-77 cDNA has three possible open reading frames which encode the amino acid sequence (SEQ ID NO:2, SEQ ID NO:7 and SEQ ID NO:11) of human Tango-77. The three potential open reading frames of SEQ ID NO:1 extend from: (1) nucleotide 356 to nucleotide 889 (SEQ ID NO:3); (2) nucleotide 389 to nucleotide 889 (SEQ ID NO:6); and (3) nucleotide 481 to nucleotide 889 (SEQ ID NO:10).

20 Figure 2 depicts an alignment of an amino acid sequence of Tango-77 (T77; SEQ ID NO:2) with IL-1RA (SEQ ID NO:14), and IL-1 β (SEQ ID NO:15).

Figure 3 depicts the genomic sequence of BAC1 (SEQ ID NO:16).

25 Figure 4 depicts the genomic sequence of BAC2 (SEQ ID NO:17).

Figure 5 depicts an amino acid sequence of an alternatively spliced form of Tango-77 (SEQ ID NO:2) as predicted by Procrustes (T77-procrustes; SEQ ID NO:18).

30 Figure 6 depicts an alignment of an amino acid sequence of an alternatively spliced form of Tango-77 (T77-procrustes; SEQ ID NO:18) with Tango-77 (SEQ ID NO:2).

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Figure 7 depicts an alignment of an amino acid sequence of an alternatively spliced form of Tango-77 (T77-procrustes; SEQ ID NO:18) with IL-1ra (SEQ ID NO:14), and IL-1 β (SEQ ID NO:15).

5 Detailed Description of the Invention

The present invention is based on the discovery of a cDNA molecule encoding human Tango-77, a member of the cytokine superfamily. The cDNA molecule encoding human Tango-77 has three possible open reading frames. The
10 three possible nucleotide open reading frames for human Tango-77 protein are shown in Figure 1 (SEQ ID NO:3, SEQ ID NO:6 and SEQ ID NO:10). The predicted amino acid sequence for the three possible Tango-77 immature proteins are also shown in
15 Figure 1 (SEQ ID NO:2, SEQ ID NO:7 or SEQ ID NO:11) and three possible mature proteins are also shown in Figure 1 (SEQ ID NO:5, SEQ ID NO:9 and SEQ ID NO:13).

The Tango-77 cDNA of Figure 1 (SEQ ID NO:1), which is approximately 989 nucleotides long including
20 untranslated regions, encodes a protein amino acid having a molecular weight of approximately 19 kDa, 18 kDa, or 14.9 kDa (excluding post-translational modifications) and the possible mature form of the protein has a molecular weight of 13 kDa. A plasmid containing a cDNA encoding
25 human Tango-77 (with the cDNA insert name of Of fthx077) was deposited with American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209 on July 2, 1998 and assigned Accession Number 98807. This deposit will be maintained under the terms
30 of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure. This deposit was made merely as a convenience for those of skill in the art and is not an

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admission that a deposit is required under 35 U.S.C. §112.

Human Tango-77 is one member of a family of molecules (the "Tango-77 family") having certain
5 conserved structural and functional features. The term "family," when referring to the protein and nucleic acid molecules of the invention, is intended to mean two or more proteins or nucleic acid molecules having a common structural domain and having sufficient amino acid or
10 nucleotide sequence identity as defined herein. Such family members can be naturally occurring and can be from either the same or different species. For example, a family can contain a first protein of human origin and a homologue of that protein of murine origin, as well as a
15 second, distinct protein of human origin and a murine homologue of that protein. Members of a family may also have common functional characteristics.

As used interchangeably herein a "Tango-77 activity", "biological activity of Tango-77" or
20 "functional activity of Tango-77", refers to an activity exerted by a Tango-77 protein, polypeptide or nucleic acid molecule on a Tango-77 responsive cell as determined *in vivo*, or *in vitro*, according to standard techniques. A Tango-77 activity can be a direct activity, such as an
25 association with a second protein, or an indirect activity, such as a cellular signaling activity mediated by interaction of the Tango-77 protein with a second protein. In a preferred embodiment, a Tango-77 activity includes at least one or more of the following
30 activities: (i) the ability to interact with proteins in the Tango-77 signalling pathway (ii) the ability to interact with a Tango-77 ligand or receptor; or (iii) the ability to interact with an intracellular target protein, (iv) the ability to interact with a protein involved in

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inflammation, and (v) the ability to bind the IL-1 receptor.

Accordingly, another embodiment of the invention features isolated Tango-77 proteins and polypeptides
5 having a Tango-77 activity.

Yet another embodiment of the invention features Tango-77 molecules which contain a signal sequence. Generally, a signal sequence (or signal peptide) is a peptide containing about 21 to 63 amino acids which
10 occurs at the extreme N-terminal end of a secretory protein. The native Tango-77 signal sequence (SEQ ID NO:4, SEQ ID NO:8, or SEQ ID NO:12) can be removed and replaced with a signal sequence from another protein. In certain host cells (e.g., mammalian host cells),
15 expression and/or secretion of Tango-77 can be increased through use of a heterologous signal sequence. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence. Alternatively, the native Tango-77 signal
20 sequence can itself be used as a heterologous signal sequence in expression systems, e.g., to facilitate the secretion of a protein of interest.

Various aspects of the invention are described in further detail in the following subsections.

25 I. Isolated Nucleic Acid Molecules

One aspect of the invention pertains to isolated nucleic acid molecules that encode Tango-77 proteins or biologically active portions thereof, as well as nucleic acid molecules sufficient for use as hybridization probes
30 to identify Tango-77-encoding nucleic acids (e.g., Tango-77 mRNA) and fragments for use as PCR primers for the amplification or mutation of Tango-77 nucleic acid molecules. As used herein, the term "nucleic acid molecule" is intended to include DNA molecules (e.g.,

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cDNA or genomic DNA) and RNA molecules (e.g., mRNA) and analogs of the DNA or RNA generated using nucleotide analogs. The nucleic acid molecule can be single-stranded or double-stranded, but preferably is double-stranded DNA.

An "isolated" nucleic acid molecule is one which is separated from other nucleic acid molecules which are present in the natural source of the nucleic acid. Preferably, an "isolated" nucleic acid is free of sequences (preferably protein encoding sequences) which naturally flank the nucleic acid (i.e., sequences located at the 5' and 3' ends of the nucleic acid) in the genomic DNA of the organism from which the nucleic acid is derived. For example, in various embodiments, the isolated Tango-77 nucleic acid molecule can contain less than about 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb or 0.1 kb of nucleotide sequences which naturally flank the nucleic acid molecule in genomic DNA of the cell from which the nucleic acid is derived. Moreover, an "isolated" nucleic acid molecule, such as a cDNA molecule, can be substantially free of other cellular material, or culture medium when produced by recombinant techniques, or substantially free of chemical precursors or other chemicals when chemically synthesized.

A nucleic acid molecule of the present invention, e.g., a nucleic acid molecule having the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or a complement of any of these nucleotide sequences, can be isolated using standard molecular biology techniques and the sequence information provided herein. Using all or a portion of the nucleic acid sequences of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or the complement thereof as a hybridization probe, Tango-77 nucleic acid molecules can be isolated using standard

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hybridization and cloning techniques (e.g., as described in Sambrook et al., eds., *Molecular Cloning: A Laboratory Manual*, 2nd ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989).

A nucleic acid of the invention can be amplified using cDNA, mRNA or genomic DNA as a template and appropriate oligonucleotide primers according to standard PCR amplification techniques. The nucleic acid so amplified can be cloned into an appropriate vector and characterized by DNA sequence analysis. Furthermore, oligonucleotides corresponding to Tango-77 nucleotide sequences can be prepared by standard synthetic techniques, e.g., using an automated DNA synthesizer.

In another preferred embodiment, an isolated nucleic acid molecule of the invention comprises a nucleic acid molecule which is a complement of the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 the cDNA of ATCC 98807, or a portion thereof. A nucleic acid molecule which is complementary to a given nucleotide sequence is one which is sufficiently complementary to the given nucleotide sequence that it can hybridize to the given nucleotide sequence thereby forming a stable duplex.

Moreover, the nucleic acid molecule of the invention can comprise only a portion of a nucleic acid sequence encoding Tango-77, for example, a fragment which can be used as a probe or primer or a fragment encoding a biologically active portion of Tango-77. The nucleotide sequence determined from the cloning of the human Tango-77 gene allows for the generation of probes and primers designed for use in identifying and/or cloning Tango-77 homologues in other cell types, e.g., from other tissues, as well as Tango-77 homologues from other mammals. The probe/primer typically comprises

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substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25,
5 more preferably about 50, 75, 100, 125, 150, 175, 200, 250, 300, 350 or 400 consecutive nucleotides of the sense or anti-sense sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807. Alternatively, the oligonucleotide can typically comprise
10 a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, preferably about 25, more preferably about 50, 75, 100, 125, 150, 175, 200, 250, 300, 350 or 400 consecutive nucleotides of the sense or anti-sense sequence of a naturally occurring
15 mutant of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

Probes based on the human Tango-77 nucleotide sequence can be used to detect transcripts or genomic sequences encoding the same or identical proteins. The
20 probe comprises a label group attached thereto, e.g., a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such probes can be used as a part of a diagnostic test kit for identifying cells or tissues which mis-express a Tango-77 protein, such as by
25 measuring a level of a Tango-77-encoding nucleic acid in a sample of cells from a subject, e.g., detecting Tango-77 mRNA levels or determining whether a genomic Tango-77 gene has been mutated or deleted.

A nucleic acid fragment encoding a "biologically
30 active portion of Tango-77" can be prepared by isolating a portion of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the nucleotide sequence of the cDNA of ATCC 98807 which encodes a polypeptide having a Tango-77 biological activity, expressing the encoded portion of
35 Tango-77 protein (e.g., by recombinant expression in

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vitro) and assessing the activity of the encoded portion of Tango-77.

The invention further encompasses nucleic acid molecules that differ from the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807 due to degeneracy of the genetic code and thus encode the same Tango-77 protein as that encoded by the nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

In addition to the human Tango-77 nucleotide sequence shown in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences of Tango-77 may exist within a population (e.g., the human population). Such genetic polymorphism in the Tango-77 gene may exist among individuals within a population due to natural allelic variation. An allele is one of a group of genes which occur alternatively at a given genetic locus. As used herein, the term "allelic variant" refers to a nucleotide sequence which occurs at a Tango-77 locus or to a polypeptide encoded by the nucleotide sequence. As used herein, the terms "gene" and "recombinant gene" refer to nucleic acid molecules comprising an open reading frame encoding a Tango-77 protein, preferably a mammalian Tango-77 protein. Such natural allelic variations can typically result in 1-5% variance in the nucleotide sequence of the Tango-77 gene. Alternative alleles can be identified by sequencing the gene of interest in a number of different individuals. This can be readily carried out by using hybridization probes to identify the same genetic locus in a variety of individuals. Any and all such nucleotide variations and resulting amino acid polymorphisms or variations in

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Tango-77 that are the result of natural allelic variation and that do not alter the functional activity of Tango-77 are intended to be within the scope of the invention.

Moreover, nucleic acid molecules encoding Tango-77
5 proteins from other species (Tango-77 homologues), which have a nucleotide sequence which differs from that of a human Tango-77, are intended to be within the scope of the invention. Nucleic acid molecules corresponding to natural allelic variants and homologues of the Tango-77
10 cDNA of the invention can be isolated based on their identity to the human Tango-77 nucleic acids disclosed herein using the human cDNAs, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.

15 Accordingly, in another embodiment, an isolated nucleic acid molecule of the invention is at least 300 (325, 350, 375, 400, 425, 450, 500, 550, 600, 650, 700, 800, or 989) nucleotides in length and hybridizes under stringent conditions to the nucleic acid molecule
20 comprising the nucleotide sequence, preferably the coding sequence, of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807.

As used herein, the term "hybridizes under stringent conditions" is intended to describe conditions
25 for hybridization and washing under which nucleotide sequences at least 60% (65%, 70%, preferably 75%) identical to each other typically remain hybridized to each other. Such stringent conditions are known to those skilled in the art and can be found in Current Protocols
30 in *Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. A preferred, non-limiting example of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45°C, followed by one or more washes in 0.2X SSC, 0.1% SDS at
35 50-65°C. Preferably, an isolated nucleic acid molecule

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of the invention that hybridizes under stringent conditions to the sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA of ATCC 98807, or the complement thereof, corresponds to a naturally-occurring
5 nucleic acid molecule. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (e.g., encodes a natural protein).

In addition to naturally-occurring allelic
10 variants of the Tango-77 sequence that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the cDNA of ATCC 98807, thereby
15 leading to changes in the amino acid sequence of the encoded Tango-77 protein, without altering the biological activity of the Tango-77 protein. Amino acid residues that are not conserved or only semiconserved among Tango-77 of various species may be non-essential for activity
20 and thus would likely be targets for alteration.

Alternatively, one can make nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues. A "non-essential" amino acid residue is a residue that can be altered from the wild-
25 type sequence of Tango-77 (e.g., the sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11 or SEQ ID NO:13) without altering the biological activity, whereas an "essential" amino acid residue is required for biological activity. For example, amino
30 acid residues that are conserved among the Tango-77 proteins of various species may be essential for activity and thus would not likely be targets for alteration, unless one wishes to reduce or alter Tango-77 activity.

Accordingly, another aspect of the invention
35 pertains to nucleic acid molecules encoding Tango-77

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proteins that contain changes in amino acid residues that are not essential for activity. Such Tango-77 proteins differ in amino acid sequence from SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 yet retain biological activity. In one embodiment, the isolated nucleic acid molecule includes a nucleotide sequence encoding a protein that includes an amino acid sequence that is at least about 45% identical, 65%, 75%, 85%, 95%, or 98% identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

An isolated nucleic acid molecule encoding a Tango-77 protein having a sequence which differs from that of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 can be created by introducing one or more nucleotide substitutions, additions or deletions into the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the cDNA of ATCC 98807 such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis. Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine,

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valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine).

5 Thus, a predicted nonessential amino acid residue in Tango-77 is preferably replaced with another amino acid residue from the same side chain family. Alternatively, mutations can be introduced randomly along all or part of a Tango-77 coding sequence, such as by saturation
10 mutagenesis, and the resultant mutants can be screened for Tango-77 biological activity to identify mutants that retain activity. Following mutagenesis, the encoded protein can be expressed recombinantly and the activity of the protein can be determined.

15 In a preferred embodiment, a mutant Tango-77 protein can be assayed for: (1) the ability to form protein:protein interactions with proteins in the Tango-77 signalling pathway; (2) the ability to bind a Tango-77 ligand or receptor; or (3) the ability to bind
20 to an intracellular target protein or (4) the ability to interact with a protein involved in inflammation or (5) the ability to bind the IL-1 receptor. In yet another preferred embodiment, a mutant Tango-77 can be assayed for the ability to modulate inflammation, asthma,
25 autoimmune diseases, and sepsis.

The present invention encompasses antisense nucleic acid molecules, i.e., molecules which are complementary to a sense nucleic acid encoding a protein, e.g., complementary to the coding strand of a double-
30 stranded cDNA molecule or complementary to an mRNA sequence. Accordingly, an antisense nucleic acid can hydrogen bond to a sense nucleic acid. The antisense nucleic acid can be complementary to an entire Tango-77 coding strand, or to only a portion thereof, e.g., all or
35 part of the protein coding region (or open reading

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frame). An antisense nucleic acid molecule can be antisense to a noncoding region of the coding strand of a nucleotide sequence encoding Tango-77. The noncoding regions ("5' and 3' untranslated regions") are the 5' and
5 3' sequences which flank the coding region and are not translated into amino acids.

Given the coding strand sequences encoding Tango-77 disclosed herein (e.g., SEQ ID NO:3, SEQ ID NO:5, or SEQ ID NO:8), antisense nucleic acids of the invention
10 can be designed according to the rules of Watson and Crick base pairing. The antisense nucleic acid molecule can be complementary to the entire coding region of Tango-77 mRNA, but more preferably is an oligonucleotide which is antisense to only a portion of the coding or
15 noncoding region of Tango-77 mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of Tango-77 mRNA, e.g., an oligonucleotide having the sequence
5'-TGCAACTTTTACAGGAAACAC-3' (SEQ ID NO:19) or
20 5'-CCTCACTTTTACCCGAGACTC-3' (SEQ ID NO:20) or
5'-GACGGGTGGTACTTAAACAA-3' (SEQ ID NO:21). An antisense oligonucleotide can be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45 or 50 nucleotides in length. An antisense nucleic acid of the invention can be
25 constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid (e.g., an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously
30 modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used.
35 Examples of modified nucleotides which can be used to

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generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (i.e., RNA transcribed from the inserted nucleic acid will be of an antisense orientation to a target nucleic acid of interest, described further in the following subsection).

The antisense nucleic acid molecules of the invention are typically administered to a subject or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a Tango-77 protein to thereby inhibit expression of the protein, e.g., by inhibiting transcription and/or translation. The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule which

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binds to DNA duplexes, through specific interactions in the major groove of the double helix. An example of a route of administration of antisense nucleic acid molecules of the invention includes direct injection at a tissue site. Alternatively, antisense nucleic acid molecules can be modified to target selected cells and then administered systemically. For example, for systemic administration, antisense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, e.g., by linking the antisense nucleic acid molecules to peptides or antibodies which bind to cell surface receptors or antigens. The antisense nucleic acid molecules can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of the antisense molecules, vector constructs in which the antisense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

An antisense nucleic acid molecule of the invention can be an α -anomeric nucleic acid molecule. An α -anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β -units, the strands run parallel to each other (Gaultier et al. (1987) *Nucleic Acids Res.* 15:6625-6641). The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (Inoue et al. (1987) *Nucleic Acids Res.* 15:6131-6148) or a chimeric RNA-DNA analogue (Inoue et al. (1987) *FEBS Lett.* 215:327-330).

The invention also encompasses ribozymes. Ribozymes are catalytic RNA molecules with ribonuclease activity which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (e.g., hammerhead

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ribozymes (described in Haselhoff and Gerlach (1988) *Nature* 334:585-591)) can be used to catalytically cleave Tango-77 mRNA transcripts to thereby inhibit translation of Tango-77 mRNA. A ribozyme having specificity for a
5 Tango-77-encoding nucleic acid can be designed based upon the nucleotide sequence of a Tango-77 cDNA disclosed herein (e.g., SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10). For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide
10 sequence of the active site is complementary to the nucleotide sequence to be cleaved in a Tango-77-encoding mRNA. See, e.g., Cech et al. U.S. Patent No. 4,987,071; and Cech et al. U.S. Patent No. 5,116,742. Alternatively, Tango-77 mRNA can be used to select a
15 catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, e.g., Bartel and Szostak (1993) *Science* 261:1411-1418.

The invention also encompasses nucleic acid molecules which form triple helical structures. For
20 example, Tango-77 gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of the Tango-77 (e.g., the Tango-77 promoter and/or enhancers) to form triple helical structures that prevent transcription of the Tango-77
25 gene in target cells. See generally, Helene (1991) *Anticancer Drug Des.* 6(6):569-84; Helene (1992) *Ann. N.Y. Acad. Sci.* 660:27-36; and Maher (1992) *Bioassays* 14(12):807-15.

In preferred embodiments, the nucleic acid
30 molecules of the invention can be modified at the base moiety, sugar moiety or phosphate backbone to improve, e.g., the stability, hybridization, or solubility of the molecule. For example, the deoxyribose phosphate backbone of the nucleic acids can be modified to generate
35 peptide nucleic acids (see Hyrup et al. (1996) *Bioorganic*

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& *Medicinal Chemistry* 4(1): 5-23). As used herein, the terms "peptide nucleic acids" or "PNAs" refer to nucleic acid mimics, e.g., DNA mimics, in which the deoxyribose phosphate backbone is replaced by a pseudopeptide backbone and only the four natural nucleobases are retained. The neutral backbone of PNAs has been shown to allow for specific hybridization to DNA and RNA under conditions of low ionic strength. The synthesis of PNA oligomers can be performed using standard solid phase peptide synthesis protocols as described in Hyrup et al. (1996) *supra*; Perry-O'Keefe et al. (1996) *Proc. Natl. Acad. Sci. USA* 93: 14670-675.

PNAs of Tango-77 can be used in therapeutic and diagnostic applications. For example, PNAs can be used as antisense or antigene agents for sequence-specific modulation of gene expression by, e.g., inducing transcription or translation arrest or inhibiting replication. PNAs of Tango-77 can also be used, e.g., in the analysis of single base pair mutations in a gene by, e.g., PNA directed PCR clamping; as artificial restriction enzymes when used in combination with other enzymes, e.g., S1 nucleases (Hyrup (1996) *supra*; or as probes or primers for DNA sequence and hybridization (Hyrup (1996) *supra*; Perry-O'Keefe et al. (1996) *Proc. Natl. Acad. Sci. USA* 93: 14670-675).

In another embodiment, PNAs of Tango-77 can be modified, e.g., to enhance their stability or cellular uptake, by attaching lipophilic or other helper groups to PNA, by the formation of PNA-DNA chimeras, or by the use of liposomes or other techniques of drug delivery known in the art. For example, PNA-DNA chimeras of Tango-77 can be generated which may combine the advantageous properties of PNA and DNA. Such chimeras allow DNA recognition enzymes, e.g., RNase H and DNA polymerases, to interact with the DNA portion while the PNA portion

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would provide high binding affinity and specificity. PNA-DNA chimeras can be linked using linkers of appropriate lengths selected in terms of base stacking, number of bonds between the nucleobases, and orientation
5 (Hyrup (1996) *supra*). The synthesis of PNA-DNA chimeras can be performed as described in Hyrup (1996) *supra* and Finn et al. (1996) *Nucleic Acids Res.* 24(17):3357-63. For example, a DNA chain can be synthesized on a solid support using standard phosphoramidite coupling chemistry
10 and modified nucleoside analogs. Compounds such as 5'-(4-methoxytrityl)amino-5'-deoxy-thymidine phosphoramidite can be used as a link between the PNA and the 5' end of DNA (Mag et al. (1989) *Nucleic Acid Res.* 17:5973-88). PNA monomers are then coupled in a stepwise manner to
15 produce a chimeric molecule with a 5' PNA segment and a 3' DNA segment (Finn et al. (1996) *Nucleic Acids Res.* 24(17):3357-63). Alternatively, chimeric molecules can be synthesized with a 5' DNA segment and a 3' PNA segment (Peterser et al. (1975) *Bioorganic Med. Chem. Lett.*
20 5:1119-11124).

In other embodiments, the oligonucleotide may include other appended groups such as peptides (e.g., for targeting host cell receptors *in vivo*), or agents facilitating transport across the cell membrane (see,
25 e.g., Letsinger et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:6553-6556; Lemaitre et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:648-652; PCT Publication No. W0 88/09810) or the blood-brain barrier (see, e.g., PCT Publication No. W0 89/10134). In addition, oligonucleotides can be
30 modified with hybridization-triggered cleavage agents (see, e.g., Krol et al. (1988) *Bio/Techniques* 6:958-976) or intercalating agents (see, e.g., Zon (1988) *Pharm. Res.* 5:539-549). To this end, the oligonucleotide may be conjugated to another molecule, e.g., a peptide,

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hybridization triggered cross-linking agent, transport agent, hybridization-triggered cleavage agent, etc.

II. Isolated Tango-77 Proteins and Anti-Tango-77 Antibodies

5 One aspect of the invention pertains to isolated Tango-77 proteins, and biologically active portions thereof, as well as polypeptide fragments suitable for use as immunogens to raise anti-Tango-77 antibodies. In one embodiment, native Tango-77 proteins can be isolated
10 from cells or tissue sources by an appropriate purification scheme using standard protein purification techniques. In another embodiment, Tango-77 proteins are produced by recombinant DNA techniques. Alternative to recombinant expression, a Tango-77 protein or polypeptide
15 can be synthesized chemically using standard peptide synthesis techniques.

 An "isolated" or "purified" protein or biologically active portion thereof is substantially free of cellular material or other contaminating proteins from
20 the cell or tissue source from which the Tango-77 protein is derived, or substantially free of chemical precursors or other chemicals when chemically synthesized. The language "substantially free of cellular material" includes preparations of Tango-77 protein in which the
25 protein is separated from cellular components of the cells from which it is isolated or recombinantly produced. Thus, Tango-77 protein that is substantially free of cellular material includes preparations of Tango-77 protein having less than about 30%, 20%, 10%, or
30 5% (by dry weight) of non-Tango-77 protein (also referred to herein as a "contaminating protein"). When the Tango-77 protein or biologically active portion thereof is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture

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medium represents less than about 20%, 10%, or 5% of the volume of the protein preparation. When Tango-77 protein is produced by chemical synthesis, it is preferably substantially free of chemical precursors or other
5 chemicals, i.e., it is separated from chemical precursors or other chemicals which are involved in the synthesis of the protein. Accordingly such preparations of Tango-77 protein have less than about 30%, 20%, 10%, 5% (by dry weight) of chemical precursors or non-Tango-77 chemicals.

10 Biologically active portions of a Tango-77 protein include peptides comprising amino acid sequences sufficiently identical to or derived from the amino acid sequence of the Tango-77 protein (e.g., the amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7,
15 SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13), which include fewer amino acids than the full length Tango-77 proteins, and exhibit at least one activity of a Tango-77 protein. Typically, biologically active portions comprise a domain or motif with at least one activity of
20 the Tango-77 protein. A biologically active portion of a Tango-77 protein can be a polypeptide which is, for example, 10, 25, 50, 100 or more amino acids in length.

Moreover, other biologically active portions, in which other regions of the protein are deleted, can be
25 prepared by recombinant techniques and evaluated for one or more of the functional activities of a native Tango-77 protein.

Preferred Tango-77 protein has the amino acid sequence shown of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7,
30 SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13. Other useful Tango-77 proteins are substantially identical to SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 and retain the functional activity of the protein of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7,
35 SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 yet differ in

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amino acid sequence due to natural allelic variation or mutagenesis. Accordingly, a useful Tango-77 protein is a protein which includes an amino acid sequence at least about 45%, preferably 55%, 65%, 75%, 85%, 95%, or 99% identical to the amino acid sequence of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13 and retains the functional activity of the Tango-77 proteins of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13. In a preferred embodiment, the Tango-77 protein retains a functional activity of the Tango-77 protein of SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, or SEQ ID NO:13.

To determine the percent identity of two amino acid sequences or of two nucleic acids, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in the sequence of a first amino acid or nucleic acid sequence for optimal alignment with a second amino or nucleic acid sequence). The amino acid residues or nucleotides at corresponding amino acid positions or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid residue or nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % identity = # of identical positions/total # of positions, e.g., overlapping x 100). Preferably, the two sequences are the same length.

The determination of percent homology between two sequences can be accomplished using a mathematical algorithm. A preferred, non-limiting example of a mathematical algorithm utilized for the comparison of two sequences is the algorithm of Karlin and Altschul (1990)

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Proc. Natl. Acad. Sci. USA 87:2264-2268, modified as in Karlin and Altschul (1993) *Proc. Natl. Acad. Sci. USA* 90:5873-5877. Such an algorithm is incorporated into the NBLAST and XBLAST programs of Altschul, et al. (1990)

5 *J. Mol. Biol.* 215:403-410. BLAST nucleotide searches can be performed with the NBLAST program, score = 100, wordlength = 12 to obtain nucleotide sequences homologous to Tango-77 nucleic acid molecules of the invention. BLAST protein searches can be performed with the XBLAST

10 program, score = 50, wordlength = 3 to obtain amino acid sequences homologous to Tango-77 protein molecules of the invention. To obtain gapped alignments for comparison purposes, Gapped BLAST can be utilized as described in Altschul et al. (1997) *Nucleic Acids Res.* 25:3389-3402.

15 When utilizing BLAST and Gapped BLAST programs, the default parameters of the respective programs (e.g., XBLAST and NBLAST) can be used. See <http://www.ncbi.nlm.nih.gov>. Another preferred, non-limiting example of a mathematical algorithm utilized for

20 the comparison of sequences is the algorithm of Myers and Miller, CABIOS (1989). Such an algorithm is incorporated into the ALIGN program (version 2.0) which is part of the GCG sequence alignment software package. When utilizing the ALIGN program for comparing amino acid sequences, a

25 PAM120 weight residue table, a gap length penalty of 12, and a gap penalty of 4 can be used.

The percent identity between two sequences can be determined using techniques similar to those described above, with or without allowing gaps. In calculating

30 percent identity, only exact matches are counted.

The invention also provides Tango-77 chimeric or fusion proteins. As used herein, a Tango-77 "chimeric protein" or "fusion protein" comprises a Tango-77 polypeptide operably linked to a non-Tango-77

35 polypeptide. A "Tango-77 polypeptide" refers to a

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polypeptide having an amino acid sequence corresponding to Tango-77 polypeptides, whereas a "non-Tango-77 polypeptide" refers to a polypeptide having an amino acid sequence corresponding to a protein which is not

5 substantially identical to the Tango-77 protein, e.g., a protein which is different from the Tango-77 protein and which is derived from the same or a different organism. Within a Tango-77 fusion protein the Tango-77 polypeptide can correspond to all or a portion of a Tango-77 protein,

10 preferably at least one biologically active portion of a Tango-77 protein. Within the fusion protein, the term "operably linked" is intended to indicate that the Tango-77 polypeptide and the non-Tango-77 polypeptide are fused in-frame to each other. The non-Tango-77

15 polypeptide can be fused to the N-terminus or C-terminus of the Tango-77 polypeptide.

One useful fusion protein is a GST-Tango-77 fusion protein in which the Tango-77 sequences are fused to the C-terminus of the GST sequences. Such fusion proteins

20 can facilitate the purification of recombinant Tango-77.

In another embodiment, the fusion protein is a Tango-77 protein containing a heterologous signal sequence at its N-terminus. For example, the native Tango-77 signal sequence (i.e., about amino acids 1 to 63

25 of SEQ ID NO:2; SEQ ID NO:4; or about amino acids 1 to 52 of SEQ ID NO:7; SEQ ID NO:8; or about amino acids 1 to 21 of SEQ ID NO:11; SEQ ID NO:12) can be removed and replaced with a signal sequence from another protein. In certain host cells (e.g., mammalian host cells), expression

30 and/or secretion of Tango-77 can be increased through use of a heterologous signal sequence. For example, the gp67 secretory sequence of the baculovirus envelope protein can be used as a heterologous signal sequence (Ausubel et al., *supra*). Other examples of eukaryotic heterologous

35 signal sequences include the secretory sequences of

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melittin and human placental alkaline phosphatase (Stratagene; La Jolla, California). In yet another example, useful prokaryotic heterologous signal sequences include the phoA secretory signal (Sambrook et al.,
5 supra) and the protein A secretory signal (Pharmacia Biotech; Piscataway, New Jersey).

In yet another embodiment, the fusion protein is an Tango-77-immunoglobulin fusion protein in which all or part of Tango-77 is fused to sequences derived from a
10 member of the immunoglobulin protein family. The Tango-77-immunoglobulin fusion proteins of the invention can be incorporated into pharmaceutical compositions and administered to a subject to inhibit an interaction between a Tango-77 ligand and a Tango-77 receptor on the
15 surface of a cell, to thereby suppress Tango-77-mediated signal transduction in vivo. The Tango-77-immunoglobulin fusion proteins can be used to affect the bioavailability of a Tango-77 cognate ligand. Inhibition of the Tango-77 ligand/Tango-77 interaction may be useful therapeutically
20 for both the treatment of inflammatory and autoimmune disorders. Moreover, the Tango-77-immunoglobulin fusion proteins of the invention can be used as immunogens to produce anti-Tango-77 antibodies in a subject, to purify Tango-77 ligands and in screening assays to identify
25 molecules which inhibit the interaction of Tango-77 with a Tango-77 receptor.

Preferably, a Tango-77 chimeric or fusion protein of the invention is produced by standard recombinant DNA techniques. For example, DNA fragments coding for the
30 different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, for example by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as
35 appropriate, alkaline phosphatase treatment to avoid

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undesirable joining, and enzymatic ligation. In another embodiment, the fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, e.g., *Current Protocols in Molecular Biology*, Ausubel et al. eds., John Wiley & Sons: 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST polypeptide). An Tango-77-encoding nucleic acid can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the Tango-77 protein.

The present invention also pertains to variants of the Tango-77 proteins (i.e., proteins having a sequence which differs from that of the Tango-77 amino acid sequence). Such variants can function as either Tango-77 agonists (mimetics) or as Tango-77 antagonists. Variants of the Tango-77 protein can be generated by mutagenesis, e.g., discrete point mutation or truncation of the Tango-77 protein. An agonist of the Tango-77 protein can retain substantially the same, or a subset, of the biological activities of the naturally occurring form of the Tango-77 protein. An antagonist of the Tango-77 protein can inhibit one or more of the activities of the naturally occurring form of the Tango-77 protein by, for example, competitively binding to a downstream or upstream member of a cellular signaling cascade which includes the Tango-77 protein. Thus, specific biological effects can be elicited by treatment with a variant of limited function. Treatment of a subject with a variant having a subset of the biological activities of the naturally occurring form of the protein can have fewer

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side effects in a subject relative to treatment with the naturally occurring form of the Tango-77 proteins.

Variants of the Tango-77 protein which function as either Tango-77 agonists (mimetics) or as Tango-77
5 antagonists can be identified by screening combinatorial libraries of mutants, e.g., truncation mutants, of the Tango-77 protein for Tango-77 protein agonist or antagonist activity. In one embodiment, a variegated library of Tango-77 variants is generated by
10 combinatorial mutagenesis at the nucleic acid level and is encoded by a variegated gene library. A variegated library of Tango-77 variants can be produced by, for example, enzymatically ligating a mixture of synthetic oligonucleotides into gene sequences such that a
15 degenerate set of potential Tango-77 sequences is expressible as individual polypeptides, or alternatively, as a set of larger fusion proteins (e.g., for phage display) containing the set of Tango-77 sequences therein. There are a variety of methods which can be
20 used to produce libraries of potential Tango-77 variants from a degenerate oligonucleotide sequence. Chemical synthesis of a degenerate gene sequence can be performed in an automatic DNA synthesizer, and the synthetic gene then ligated into an appropriate expression vector. Use
25 of a degenerate set of genes allows for the provision, in one mixture, of all of the sequences encoding the desired set of potential Tango-77 sequences. Methods for synthesizing degenerate oligonucleotides are known in the art (see, e.g., Narang (1983) *Tetrahedron* 39:3; Itakura
30 et al. (1984) *Annu. Rev. Biochem.* 53:323; Itakura et al. (1984) *Science* 198:1056; Ike et al. (1983) *Nucleic Acid Res.* 11:477).

In addition, libraries of fragments of the Tango-77 protein coding sequence can be used to generate
35 a variegated population of Tango-77 fragments for

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screening and subsequent selection of variants of a Tango-77 protein. In one embodiment, a library of coding sequence fragments can be generated by treating a double stranded PCR fragment of a Tango-77 coding sequence with
5 a nuclease under conditions wherein nicking occurs only about once per molecule, denaturing the double stranded DNA, renaturing the DNA to form double stranded DNA which can include sense/antisense pairs from different nicked products, removing single stranded portions from reformed
10 duplexes by treatment with S1 nuclease, and ligating the resulting fragment library into an expression vector. By this method, an expression library can be derived which encodes N-terminal and internal fragments of various sizes of the Tango-77 protein.

15 Several techniques are known in the art for screening gene products of combinatorial libraries made by point mutations or truncation, and for screening cDNA libraries for gene products having a selected property. Such techniques are adaptable for rapid screening of the
20 gene libraries generated by the combinatorial mutagenesis of Tango-77 proteins. The most widely used techniques, which are amenable to high through-put analysis, for screening large gene libraries typically include cloning the gene library into replicable expression vectors,
25 transforming appropriate cells with the resulting library of vectors, and expressing the combinatorial genes under conditions in which detection of a desired activity facilitates isolation of the vector encoding the gene whose product was detected. Recursive ensemble
30 mutagenesis (REM), a technique which enhances the frequency of functional mutants in the libraries, can be used in combination with the screening assays to identify Tango-77 variants (Arkin and Yourvan (1992) *Proc. Natl. Acad. Sci. USA* 89:7811-7815; Delgrave et al. (1993)
35 *Protein Engineering* 6(3):327-331).

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An isolated Tango-77 protein, or a portion or fragment thereof, can be used as an immunogen to generate antibodies that bind Tango-77 using standard techniques for polyclonal and monoclonal antibody preparation. The
5 full-length Tango-77 protein can be used or, alternatively, the invention provides antigenic peptide fragments of Tango-77 for use as immunogens. The antigenic peptide of Tango-77 comprises at least 8 (preferably 10, 15, 20, or 30) amino acid residues of the
10 amino acid sequence shown in SEQ ID NO:2, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11 or SEQ ID NO:13 and encompasses an epitope of Tango-77 such that an antibody raised against the peptide forms a specific immune complex with Tango-77.

15 A Tango-77 immunogen typically is used to prepare antibodies by immunizing a suitable subject (e.g., rabbit, goat, mouse or other mammal) with the immunogen. An appropriate immunogenic preparation can contain, for example, recombinantly expressed Tango-77 protein or a
20 chemically synthesized Tango-77 polypeptide. The preparation can further include an adjuvant, such as Freund's complete or incomplete adjuvant, or similar immunostimulatory agent. Immunization of a suitable subject with an immunogenic Tango-77 preparation induces
25 a polyclonal anti-Tango-77 antibody response.

Accordingly, another aspect of the invention pertains to anti-Tango-77 antibodies. The term "antibody" as used herein refers to immunoglobulin molecules and immunologically active portions of
30 immunoglobulin molecules, i.e., molecules that contain an antigen binding site which specifically binds an antigen, such as Tango-77. A molecule which specifically binds to Tango-77 is a molecule which binds Tango-77, but does not substantially bind other molecules in a sample, e.g., a
35 biological sample, which naturally contains Tango-77.

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Examples of immunologically active portions of immunoglobulin molecules include F(ab) and F(ab')₂ fragments which can be generated by treating the antibody with an enzyme such as pepsin. The invention provides
5 polyclonal and monoclonal antibodies that bind Tango-77. The term "monoclonal antibody" or "monoclonal antibody composition", as used herein, refers to a population of antibody molecules that contain only one species of an antigen binding site capable of immunoreacting with a
10 particular epitope of Tango-77. A monoclonal antibody composition thus typically displays a single binding affinity for a particular Tango-77 protein with which it immunoreacts.

Polyclonal anti-Tango-77 antibodies can be
15 prepared as described above by immunizing a suitable subject with a Tango-77 immunogen. The anti-Tango-77 antibody titer in the immunized subject can be monitored over time by standard techniques, such as with an enzyme linked immunosorbent assay (ELISA) using immobilized
20 Tango-77. If desired, the antibody molecules directed against Tango-77 can be isolated from the mammal (e.g., from the blood) and further purified by well-known techniques, such as protein A chromatography to obtain the IgG fraction. At an appropriate time after
25 immunization, e.g., when the anti-Tango-77 antibody titers are highest, antibody-producing cells can be obtained from the subject and used to prepare monoclonal antibodies by standard techniques, such as the hybridoma technique originally described by Kohler and Milstein
30 (1975) *Nature* 256:495-497, the human B cell hybridoma technique (Kozbor et al. (1983) *Immunol Today* 4:72), the EBV-hybridoma technique (Cole et al. (1985), *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, Inc., pp. 77-96) or trioma techniques. The technology for
35 producing hybridomas is well known (see generally Current

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Protocols in Immunology (1994) Coligan et al. (eds.) John Wiley & Sons, Inc., New York, NY). Briefly, an immortal cell line (typically a myeloma) is fused to lymphocytes (typically splenocytes) from a mammal immunized with a
5 Tango-77 immunogen as described above, and the culture supernatants of the resulting hybridoma cells are screened to identify a hybridoma producing a monoclonal antibody that binds Tango-77.

Any of the many well known protocols used for
10 fusing lymphocytes and immortalized cell lines can be applied for the purpose of generating an anti-Tango-77 monoclonal antibody (see, e.g., Current Protocols in Immunology, supra; Galfre et al. (1977) *Nature* 266:55052; R.H. Kenneth, in *Monoclonal Antibodies: A New Dimension*
15 *In Biological Analyses*, Plenum Publishing Corp., New York, New York (1980); and Lerner (1981) *Yale J. Biol. Med.*, 54:387-402. Moreover, the ordinarily skilled worker will appreciate that there are many variations of such methods which also would be useful. Typically, the
20 immortal cell line (e.g., a myeloma cell line) is derived from the same mammalian species as the lymphocytes. For example, murine hybridomas can be made by fusing lymphocytes from a mouse immunized with an immunogenic preparation of the present invention with an immortalized
25 mouse cell line, e.g., a myeloma cell line that is sensitive to culture medium containing hypoxanthine, aminopterin and thymidine ("HAT medium"). Any of a number of myeloma cell lines can be used as a fusion partner according to standard techniques, e.g., the P3-
30 NS1/1-Ag4-1, P3-x63-Ag8.653 or Sp2/O-Ag14 myeloma lines. These myeloma lines are available from ATCC. Typically, HAT-sensitive mouse myeloma cells are fused to mouse splenocytes using polyethylene glycol ("PEG"). Hybridoma cells resulting from the fusion are then selected using
35 HAT medium, which kills unfused and unproductively fused

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myeloma cells (unfused splenocytes die after several days because they are not transformed). Hybridoma cells producing a monoclonal antibody of the invention are detected by screening the hybridoma culture supernatants
5 for antibodies that bind Tango-77, e.g., using a standard ELISA assay.

Alternative to preparing monoclonal antibody-secreting hybridomas, a monoclonal anti-Tango-77 antibody can be identified and isolated by screening a recombinant
10 combinatorial immunoglobulin library (e.g., an antibody phage display library) with Tango-77 to thereby isolate immunoglobulin library members that bind Tango-77. Kits for generating and screening phage display libraries are commercially available (e.g., the Pharmacia Recombinant
15 *Phage Antibody System*, Catalog No. 27-9400-01; and the Stratagene *SurfZAP™ Phage Display Kit*, Catalog No. 240612). Additionally, examples of methods and reagents particularly amenable for use in generating and screening antibody display library can be found in, for example,
20 U.S. Patent No. 5,223,409; PCT Publication No. WO 92/18619; PCT Publication No. WO 91/17271; PCT Publication No. WO 92/20791; PCT Publication No. WO 92/15679; PCT Publication No. WO 93/01288; PCT Publication No. WO 92/01047; PCT Publication No. WO
25 92/09690; PCT Publication No. WO 90/02809; Fuchs et al. (1991) *Bio/Technology* 9:1370-1372; Hay et al. (1992) *Hum. Antibod. Hybridomas* 3:81-85; Huse et al. (1989) *Science* 246:1275-1281; Griffiths et al. (1993) *EMBO J* 12:725-734.

Additionally, recombinant anti-Tango-77
30 antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which can be made using standard recombinant DNA techniques, are within the scope of the invention. Such chimeric and humanized monoclonal antibodies can be
35 produced by recombinant DNA techniques known in the art,

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for example using methods described in PCT Publication No. WO 87/02671; European Patent Application 184,187; European Patent Application 171,496; European Patent Application 173,494; PCT Publication No. WO 86/01533; 5 U.S. Patent No. 4,816,567; European Patent Application 125,023; Better et al. (1988) *Science* 240:1041-1043; Liu et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:3439-3443; Liu et al. (1987) *J. Immunol.* 139:3521-3526; Sun et al. (1987) *Proc. Natl. Acad. Sci. USA* 84:214-218; Nishimura 10 et al. (1987) *Canc. Res.* 47:999-1005; Wood et al. (1985) *Nature* 314:446-449; and Shaw et al. (1988) *J. Natl. Cancer Inst.* 80:1553-1559; Morrison (1985) *Science* 229:1202-1207; Oi et al. (1986) *Bio/Techniques* 4:214; U.S. Patent 5,225,539; Jones et al. (1986) *Nature* 15 321:552-525; Verhoeyan et al. (1988) *Science* 239:1534; and Beidler et al. (1988) *J. Immunol.* 141:4053-4060.

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Such antibodies can be produced using transgenic mice 20 which are incapable of expressing endogenous immunoglobulin heavy and light chains genes, but which can express human heavy and light chain genes. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of Tango-77. 25 Monoclonal antibodies directed against the antigen can be obtained using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic 30 mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar (1995, *Int. Rev. Immunol.* 13:65-93). For a detailed discussion 35 of this technology for producing human antibodies and

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human monoclonal antibodies and protocols for producing such antibodies, see, e.g., U.S. Patent 5,625,126; U.S. Patent 5,633,425; U.S. Patent 5,569,825; U.S. Patent 5,661,016; and U.S. Patent 5,545,806. In addition,
5 companies such as Abgenix, Inc. (Freemont, CA), can be engaged to provide human antibodies directed against a selected antigen using technology similar to the described above.

Completely human antibodies which recognize a
10 selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a murine antibody, is used to guide the selection of a completely human antibody recognizing the same epitope.

15 First, a non-human monoclonal antibody which binds a selected antigen (epitope), e.g., an antibody which inhibits Tango-77 activity, is identified. The heavy chain and the light chain of the non-human antibody are cloned and used to create phage display Fab fragments.
20 For example, the heavy chain gene can be cloned into a plasmid vector so that the heavy chain can be secreted from bacteria. The light chain gene can be cloned into a phage coat protein gene so that the light chain can be expressed on the surface of phage. A repertoire (random
25 collection) of human light chains fused to phage is used to infect the bacteria which express the non-human heavy chain. The resulting progeny phage display hybrid antibodies (human light chain/non-human heavy chain). The selected antigen is used in a panning screen to
30 select phage which bind the selected antigen. Several rounds of selection may be required to identify such phage. Next, human light chain genes are isolated from the selected phage which bind the selected antigen. These selected human light chain genes are then used to
35 guide the selection of human heavy chain genes as

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follows. The selected human light chain genes are inserted into vectors for expression by bacteria. Bacteria expressing the selected human light chains are infected with a repertoire of human heavy chains fused to
5 phage. The resulting progeny phage display human antibodies (human light chain/human heavy chain).

Next, the selected antigen is used in a panning screen to select phage which bind the selected antigen. The phage selected in this step display completely human
10 antibody which recognize the same epitope recognized by the original selected, non-human monoclonal antibody. The genes encoding both the heavy and light chains are readily isolated and be further manipulated for production of human antibody. This technology is
15 described by Jespers et al. (1994, *Bio/technology* 12:899-903).

An anti-Tango-77 antibody (e.g., monoclonal antibody) can be used to isolate Tango-77 by standard techniques, such as affinity chromatography or
20 immunoprecipitation. An anti-Tango-77 antibody can facilitate the purification of natural Tango-77 from cells and of recombinantly produced Tango-77 expressed in host cells. Moreover, an anti-Tango-77 antibody can be used to detect Tango-77 protein (e.g., in a cellular
25 lysate or cell supernatant) in order to evaluate the abundance and pattern of expression of the Tango-77 protein. Anti-Tango-77 antibodies can be used diagnostically to monitor protein levels in tissue as part of a clinical testing procedure, e.g., to, for
30 example, determine the efficacy of a given treatment regimen. Detection can be facilitated by coupling the antibody to a detectable substance. Examples of detectable substances include various enzymes, prosthetic groups, fluorescent materials, luminescent materials,
35 bioluminescent materials, and radioactive materials.

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Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, β -galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and
5 avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of
10 bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ^{125}I , ^{131}I , ^{35}S or ^3H .

III. Recombinant Expression Vectors and Host Cells

Another aspect of the invention pertains to
15 vectors, preferably expression vectors, containing a nucleic acid molecule encoding Tango-77 (or a portion thereof). As used herein, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. One type of
20 vector is a "plasmid", which refers to a circular double stranded DNA loop into which additional DNA segments can be ligated. Another type of vector is a viral vector, wherein additional DNA segments can be ligated into the viral genome. Certain vectors are capable of autonomous
25 replication in a host cell into which they are introduced (e.g., bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) are integrated into the genome of a host cell upon
30 introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors, expression vectors, are capable of directing the expression of genes to which they are operably linked. In general, expression vectors of utility in recombinant

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DNA techniques are often in the form of plasmids (vectors). However, the invention is intended to include such other forms of expression vectors, such as viral vectors (e.g., replication defective retroviruses, adenoviruses and adeno-associated viruses), which serve equivalent functions.

The recombinant expression vectors of the invention comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory sequences, selected on the basis of the host cells to be used for expression, which is operably linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory sequence(s) in a manner which allows for expression of the nucleotide sequence (e.g., in an *in vitro* transcription/translation system or in a host cell when the vector is introduced into the host cell). The term "regulatory sequence" is intended to include promoters, enhancers and other expression control elements (e.g., polyadenylation signals). Such regulatory sequences are described, for example, in Goeddel; *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990). Regulatory sequences include those which direct constitutive expression of a nucleotide sequence in many types of host cell and those which direct expression of the nucleotide sequence only in certain host cells (e.g., tissue-specific regulatory sequences). It will be appreciated by those skilled in the art that the design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, etc. The expression

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vectors of the invention can be introduced into host cells to thereby produce proteins or peptides, including fusion proteins or peptides, encoded by nucleic acids as described herein (e.g., Tango-77 proteins, mutant forms
5 of Tango-77, fusion proteins, etc.).

The recombinant expression vectors of the invention can be designed for expression of Tango-77 in prokaryotic or eukaryotic cells, e.g., bacterial cells such as *E. coli*, insect cells (using baculovirus
10 expression vectors), yeast cells or mammalian cells. Suitable host cells are discussed further in Goeddel, *Gene Expression Technology: Methods in Enzymology* 185, Academic Press, San Diego, CA (1990). Alternatively, the recombinant expression vector can be transcribed and
15 translated *in vitro*, for example using T7 promoter regulatory sequences and T7 polymerase.

Expression of proteins in prokaryotes is most often carried out in *E. coli* with vectors containing constitutive or inducible promoters directing the
20 expression of either fusion or non-fusion proteins. Fusion vectors add a number of amino acids to a protein encoded therein, usually to the amino terminus of the recombinant protein. Such fusion vectors typically serve three purposes: 1) to increase expression of recombinant
25 protein; 2) to increase the solubility of the recombinant protein; and 3) to aid in the purification of the recombinant protein by acting as a ligand in affinity purification. Often, in fusion expression vectors, a proteolytic cleavage site is introduced at the junction
30 of the fusion moiety and the recombinant protein to enable separation of the recombinant protein from the fusion moiety subsequent to purification of the fusion protein. Such enzymes, and their cognate recognition sequences, include Factor Xa, thrombin and enterokinase.
35 Typical fusion expression vectors include pGEX (Pharmacia

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Biotech Inc; Smith and Johnson (1988) *Gene* 67:31-40),
pMAL (New England Biolabs, Beverly, MA) and pRIT5
(Pharmacia, Piscataway, NJ) which fuse glutathione S-
transferase (GST), maltose E binding protein, or protein
5 A, respectively, to the target recombinant protein.

Examples of suitable inducible non-fusion *E. coli*
expression vectors include pTrc (Amann et al. (1988) *Gene*
69:301-315) and pET 11d (Studier et al., *Gene Expression*
Technology: Methods in Enzymology 185, Academic Press,
10 San Diego, California (1990) 60-89). Target gene
expression from the pTrc vector relies on host RNA
polymerase transcription from a hybrid trp-lac fusion
promoter. Target gene expression from the pET 11d vector
relies on transcription from a T7 gnl0-lac fusion
15 promoter mediated by a coexpressed viral RNA polymerase
(T7 gnl). This viral polymerase is supplied by host
strains BL21(DE3) or HMS174(DE3) from a resident λ
prophage harboring a T7 gnl gene under the
transcriptional control of the lacUV 5 promoter.

20 One strategy to maximize recombinant protein
expression in *E. coli* is to express the protein in a host
bacteria with an impaired capacity to proteolytically
cleave the recombinant protein (Gottesman, *Gene*
Expression Technology: Methods in Enzymology 185,
25 Academic Press, San Diego, California (1990) 119-128).
Another strategy is to alter the nucleic acid sequence of
the nucleic acid to be inserted into an expression vector
so that the individual codons for each amino acid are
those preferentially utilized in *E. coli* (Wada et al.
30 (1992) *Nucleic Acids Res.* 20:2111-2118). Such alteration
of nucleic acid sequences of the invention can be carried
out by standard DNA synthesis techniques.

In another embodiment, the Tango-77 expression
vector is a yeast expression vector. Examples of vectors
35 for expression in yeast *S. cerevisiae* include pYepSec1

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(Baldari et al. (1987) *EMBO J.* 6:229-234), pMFa (Kurjan and Herskowitz (1982) *Cell* 30:933-943), pJRY88 (Schultz et al. (1987) *Gene* 54:113-123), pYES2 (Invitrogen Corporation, San Diego, CA), and picZ (Invitrogen Corp,
5 San Diego, CA).

Alternatively, Tango-77 can be expressed in insect cells using baculovirus expression vectors. Baculovirus vectors available for expression of proteins in cultured insect cells (e.g., Sf 9 cells) include the pAc series
10 (Smith et al. (1983) *Mol. Cell Biol.* 3:2156-2165) and the pVL series (Lucklow and Summers (1989) *Virology* 170:31-39).

In yet another embodiment, a nucleic acid of the invention is expressed in mammalian cells using a
15 mammalian expression vector. Examples of mammalian expression vectors include pCDM8 (Seed (1987) *Nature* 329:840) and pMT2PC (Kaufman et al. (1987) *EMBO J.* 6:187-195). When used in mammalian cells, the expression vector's control functions are often provided by viral
20 regulatory elements. For example, commonly used promoters are derived from polyoma, Adenovirus 2, cytomegalovirus and Simian Virus 40. For other suitable expression systems for both prokaryotic and eukaryotic cells see chapters 16 and 17 of Sambrook et al. (*supra*).

25 In another embodiment, the recombinant mammalian expression vector is capable of directing expression of the nucleic acid preferentially in a particular cell type (e.g., tissue-specific regulatory elements are used to express the nucleic acid). Tissue-specific regulatory
30 elements are known in the art. Non-limiting examples of suitable tissue-specific promoters include the albumin promoter (liver-specific; Pinkert et al. (1987) *Genes Dev.* 1:268-277), lymphoid-specific promoters (Calame and Eaton (1988) *Adv. Immunol.* 43:235-275), in particular
35 promoters of T cell receptors (Winoto and Baltimore

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(1989) *EMBO J.* 8:729-733) and immunoglobulins (Banerji et al. (1983) *Cell* 33:729-740; Queen and Baltimore (1983) *Cell* 33:741-748), neuron-specific promoters (e.g., the neurofilament promoter; Byrne and Ruddle (1989) *Proc. Natl. Acad. Sci. USA* 86:5473-5477), pancreas-specific promoters (Edlund et al. (1985) *Science* 230:912-916), and mammary gland-specific promoters (e.g., milk whey promoter; U.S. Patent No. 4,873,316 and European Application Publication No. 264,166). Developmentally-regulated promoters are also encompassed, for example the murine hox promoters (Kessel and Gruss (1990) *Science* 249:374-379) and the α -fetoprotein promoter (Campes and Tilghman (1989) *Genes Dev.* 3:537-546).

The invention further provides a recombinant expression vector comprising a DNA molecule of the invention cloned into the expression vector in an antisense orientation. That is, the DNA molecule is operably linked to a regulatory sequence in a manner which allows for expression (by transcription of the DNA molecule) of an RNA molecule which is antisense to Tango-77 mRNA. Regulatory sequences operably linked to a nucleic acid cloned in the antisense orientation can be chosen which direct the continuous expression of the antisense RNA molecule in a variety of cell types, for instance viral promoters and/or enhancers, or regulatory sequences can be chosen which direct constitutive, tissue specific or cell type specific expression of antisense RNA. The antisense expression vector can be in the form of a recombinant plasmid, phagemid or attenuated virus in which antisense nucleic acids are produced under the control of a high efficiency regulatory region, the activity of which can be determined by the cell type into which the vector is introduced. For a discussion of the regulation of gene expression using antisense genes see

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Weintraub et al. (*Reviews - Trends in Genetics*, Vol. 1(1) 1986).

Another aspect of the invention pertains to host cells into which a recombinant expression vector of the invention has been introduced. The terms "host cell" and "recombinant host cell" are used interchangeably herein. It is understood that such terms refer not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

A host cell can be any prokaryotic or eukaryotic cell. For example, Tango-77 protein can be expressed in bacterial cells such as *E. coli*, insect cells, yeast or mammalian cells (such as Chinese hamster ovary cells (CHO) or COS cells). Other suitable host cells are known to those skilled in the art.

Vector DNA can be introduced into prokaryotic or eukaryotic cells via conventional transformation or transfection techniques. As used herein, the terms "transformation" and "transfection" are intended to refer to a variety of art-recognized techniques for introducing foreign nucleic acid (e.g., DNA) into a host cell, including calcium phosphate or calcium chloride coprecipitation, DEAE-dextran-mediated transfection, lipofection, or electroporation. Suitable methods for transforming or transfecting host cells can be found in Sambrook, et al. (*supra*), and other laboratory manuals.

For stable transfection of mammalian cells, it is known that, depending upon the expression vector and transfection technique used, only a small fraction of cells may integrate the foreign DNA into their genome.

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In order to identify and select these integrants, a gene that encodes a selectable marker (e.g., for resistance to antibiotics) is generally introduced into the host cells along with the gene of interest. Preferred selectable
5 markers include those which confer resistance to drugs, such as G418, hygromycin and methotrexate. Nucleic acid encoding a selectable marker can be introduced into a host cell on the same vector as that encoding Tango-77 or can be introduced on a separate vector. Cells stably
10 transfected with the introduced nucleic acid can be identified by drug selection (e.g., cells that have incorporated the selectable marker gene will survive, while the other cells die).

A host cell of the invention, such as a
15 prokaryotic or eukaryotic host cell in culture, can be used to produce (i.e., express) Tango-77 protein. Accordingly, the invention further provides methods for producing Tango-77 protein using the host cells of the invention. In one embodiment, the method comprises
20 culturing the host cell of invention (into which a recombinant expression vector encoding Tango-77 has been introduced) in a suitable medium such that Tango-77 protein is produced. In another embodiment, the method further comprises isolating Tango-77 from the medium or
25 the host cell.

The host cells of the invention can also be used to produce nonhuman transgenic animals. For example, in one embodiment, a host cell of the invention is a fertilized oocyte or an embryonic stem cell into which
30 Tango-77-coding sequences have been introduced. Such host cells can then be used to create non-human transgenic animals in which exogenous Tango-77 sequences have been introduced into their genome or homologous recombinant animals in which endogenous Tango-77
35 sequences have been altered. Such animals are useful for

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studying the function and/or activity of Tango-77 and for identifying and/or evaluating modulators of Tango-77 activity. As used herein, a "transgenic animal" is a non-human animal, preferably a mammal, more preferably a rodent such as a rat or mouse, in which one or more of the cells of the animal includes a transgene. Other examples of transgenic animals include non-human primates, sheep, dogs, cows, goats, chickens, amphibians, etc. A transgene is exogenous DNA which is integrated into the genome of a cell from which a transgenic animal develops and which remains in the genome of the mature animal, thereby directing the expression of an encoded gene product in one or more cell types or tissues of the transgenic animal. As used herein, an "homologous recombinant animal" is a non-human animal, preferably a mammal, more preferably a mouse, in which an endogenous Tango-77 gene has been altered by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell of the animal, e.g., an embryonic cell of the animal, prior to development of the animal.

A transgenic animal of the invention can be created by introducing Tango-77-encoding nucleic acid into the male pronuclei of a fertilized oocyte, e.g., by microinjection, retroviral infection, and allowing the oocyte to develop in a pseudopregnant female foster animal. The Tango-77 cDNA sequence e.g., that of (SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6; SEQ ID NO:10 or the cDNA of ATCC 98807) can be introduced as a transgene into the genome of a non-human animal. Alternatively, a nonhuman homologue of the human Tango-77 gene, such as a mouse Tango-77 gene, can be isolated based on hybridization to the human Tango-77 cDNA and used as a transgene. Intronic sequences and polyadenylation signals can also be included in the transgene to increase the efficiency

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of expression of the transgene. A tissue-specific regulatory sequence(s) can be operably linked to the Tango-77 transgene to direct expression of Tango-77 protein to particular cells. Methods for generating

5 transgenic animals via embryo manipulation and microinjection, particularly animals such as mice, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009, U.S. Patent No. 4,873,191 and in Hogan, *Manipulating the*

10 *Mouse Embryo* (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y., 1986). Similar methods are used for production of other transgenic animals. A transgenic founder animal can be identified based upon the presence of the Tango-77 transgene in its genome and/or expression

15 of Tango-77 mRNA in tissues or cells of the animals. A transgenic founder animal can then be used to breed additional animals carrying the transgene. Moreover, transgenic animals carrying a transgene encoding Tango-77 can further be bred to other transgenic animals carrying

20 other transgenes.

To create an homologous recombinant animal, a vector is prepared which contains at least a portion of a Tango-77 gene (e.g., a human or a non-human homolog of the Tango-77 gene, e.g., a murine Tango-77 gene) into

25 which a deletion, addition or substitution has been introduced to thereby alter, e.g., functionally disrupt, the Tango-77 gene. In a preferred embodiment, the vector is designed such that, upon homologous recombination, the endogenous Tango-77 gene is functionally disrupted (i.e.,

30 no longer encodes a functional protein; also referred to as a "knock out" vector). Alternatively, the vector can be designed such that, upon homologous recombination, the endogenous Tango-77 gene is mutated or otherwise altered but still encodes functional protein (e.g., the

35 upstream regulatory region can be altered to thereby

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alter the expression of the endogenous Tango-77 protein). In the homologous recombination vector, the altered portion of the Tango-77 gene is flanked at its 5' and 3' ends by additional nucleic acid of the Tango-77 gene to
5 allow for homologous recombination to occur between the exogenous Tango-77 gene carried by the vector and an endogenous Tango-77 gene in an embryonic stem cell. The additional flanking Tango-77 nucleic acid is of sufficient length for successful homologous recombination
10 with the endogenous gene. Typically, several kilobases of flanking DNA (both at the 5' and 3' ends) are included in the vector (see, e.g., Thomas and Capecchi (1987) *Cell* 51:503 for a description of homologous recombination vectors). The vector is introduced into an embryonic
15 stem cell line (e.g., by electroporation) and cells in which the introduced Tango-77 gene has homologously recombined with the endogenous Tango-77 gene are selected (see, e.g., Li et al. (1992) *Cell* 69:915). The selected cells are then injected into a blastocyst of an animal
20 (e.g., a mouse) to form aggregation chimeras (see, e.g., Bradley in *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, Robertson, ed. (IRL, Oxford, 1987) pp. 113-152). A chimeric embryo can then be implanted into a suitable pseudopregnant female foster animal and
25 the embryo brought to term. Progeny harboring the homologously recombined DNA in their germ cells can be used to breed animals in which all cells of the animal contain the homologously recombined DNA by germline transmission of the transgene. Methods for constructing
30 homologous recombination vectors and homologous recombinant animals are described further in Bradley (1991) *Current Opinion in Bio/Technology* 2:823-829 and in PCT Publication Nos. WO 90/11354, WO 91/01140, WO 92/0968, and WO 93/04169.

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In another embodiment, transgenic non-human animals can be produced which contain selected systems which allow for regulated expression of the transgene. One example of such a system is the *cre/loxP* recombinase system of bacteriophage P1. For a description of the *cre/loxP* recombinase system, see, e.g., Lakso et al. (1992) *Proc. Natl. Acad. Sci. USA* 89:6232-6236. Another example of a recombinase system is the FLP recombinase system of *Saccharomyces cerevisiae* (O'Gorman et al. (1991) *Science* 251:1351-1355. If a *cre/loxP* recombinase system is used to regulate expression of the transgene, animals containing transgenes encoding both the Cre recombinase and a selected protein are required. Such animals can be provided through the construction of "double" transgenic animals, e.g., by mating two transgenic animals, one containing a transgene encoding a selected protein and the other containing a transgene encoding a recombinase.

Clones of the non-human transgenic animals described herein can also be produced according to the methods described in Wilmut et al. (1997) *Nature* 385:810-813 and PCT Publication Nos. WO 97/07668 and WO 97/07669. In brief, a cell, e.g., a somatic cell, from the transgenic animal can be isolated and induced to exit the growth cycle and enter G₀ phase. The quiescent cell can then be fused, e.g., through the use of electrical pulses, to an enucleated oocyte from an animal of the same species from which the quiescent cell is isolated. The reconstructed oocyte is then cultured such that it develops to morula or blastocyte and then transferred to pseudopregnant female foster animal. The offspring borne of this female foster animal will be a clone of the animal from which the cell, e.g., the somatic cell, is isolated.

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IV. Pharmaceutical Compositions

The Tango-77 nucleic acid molecules, Tango-77 proteins, and anti-Tango-77 antibodies (also referred to herein as "active compounds") of the invention can be
5 incorporated into pharmaceutical compositions suitable for administration. Such compositions typically comprise the nucleic acid molecule, protein, or antibody and a pharmaceutically acceptable carrier. As used herein the language "pharmaceutically acceptable carrier" is
10 intended to include any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, and the like, compatible with pharmaceutical administration. The use of such media and agents for pharmaceutically active
15 substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active compound, use thereof in the compositions is contemplated. Supplementary active compounds can also be incorporated into the compositions.

20 A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Examples of routes of administration include parenteral, (e.g. intravenous, intradermal, subcutaneous) (e.g., oral inhalation), transdermal
25 (topical), transmucosal, and rectal administration. Solutions or suspensions used for parenteral, intradermal, or subcutaneous application can include the following components: a sterile diluent such as water for injection, saline solution, fixed oils, polyethylene
30 glycols, glycerine, propylene glycol or other synthetic solvents; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as
35 acetates, citrates or phosphates and agents for the

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adjustment of tonicity such as sodium chloride or dextrose. pH can be adjusted with acids or bases, such as hydrochloric acid or sodium hydroxide. The parenteral preparation can be enclosed in ampoules, disposable
5 syringes or multiple dose vials made of glass or plastic.

Pharmaceutical compositions suitable for injectable use include sterile aqueous solutions (where water soluble) or dispersions and sterile powders for the extemporaneous preparation of sterile injectable
10 solutions or dispersions. For intravenous administration, suitable carriers include physiological saline, bacteriostatic water, Cremophor EL™ (BASF; Parsippany, NJ) or phosphate buffered saline (PBS). In all cases, the composition must be sterile and should be
15 fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing,
20 for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), and suitable mixtures thereof. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance
25 of the required particle size in the case of dispersion and by the use of surfactants. Prevention of the action of microorganisms can be achieved by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, ascorbic acid,
30 thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars, polyalcohols such as mannitol, sorbitol, sodium chloride in the composition. Prolonged absorption of the injectable compositions can be brought about by including

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in the composition an agent which delays absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions can be prepared by incorporating the active compound (e.g., a Tango-77 protein or anti-Tango-77 antibody) in the required amount in an appropriate solvent with one or a combination of ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the active compound into a sterile vehicle which contains a basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and freeze-drying which yields a powder of the active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

Oral compositions generally include an inert diluent or an edible carrier. They can be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Oral compositions can also be prepared using a fluid carrier for use as a mouthwash, wherein the compound in the fluid carrier is applied orally and swished and expectorated or swallowed. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition. The tablets, pills, capsules, troches and the like can contain any of the following ingredients, or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a

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glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

5 For administration by inhalation, the compounds are delivered in the form of an aerosol spray from a pressurized container or dispenser which contains a suitable propellant, e.g., a gas such as carbon dioxide, or a nebulizer.

10 Systemic administration can also be by transmucosal or transdermal means. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used in the formulation. Such penetrants are generally known in the art, and
15 include, for example, for transmucosal administration, detergents, bile salts, and fusidic acid derivatives. Transmucosal administration can be accomplished through the use of nasal sprays or suppositories. For
20 transdermal administration, the active compounds are formulated into ointments, salves, gels, or creams as generally known in the art.

 The compounds can also be prepared in the form of suppositories (e.g., with conventional suppository bases such as cocoa butter and other glycerides) or retention
25 enemas for rectal delivery.

 In one embodiment, the active compounds are prepared with carriers that will protect the compound against rapid elimination from the body, such as a controlled release formulation, including implants and
30 microencapsulated delivery systems. Biodegradable, biocompatible polymers can be used, such as ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, and polylactic acid. Methods for preparation of such formulations will be apparent to
35 those skilled in the art. The materials can also be

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obtained commercially from Alza Corporation and Nova Pharmaceuticals, Inc. Liposomal suspensions (including liposomes targeted to infected cells with monoclonal antibodies to viral antigens) can also be used as
5 pharmaceutically acceptable carriers. These can be prepared according to methods known to those skilled in the art, for example, as described in U.S. Patent No. 4,522,811.

It is especially advantageous to formulate oral or
10 parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subject to be treated; each unit containing a predetermined quantity of active
15 compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the dosage unit forms of the invention are dictated by and directly dependent on the unique characteristics of the active compound and the
20 particular therapeutic effect to be achieved, and the limitations inherent in the art of compounding such an active compound for the treatment of individuals.

The nucleic acid molecules of the invention can be inserted into vectors and used as gene therapy vectors.
25 Gene therapy vectors can be delivered to a subject by, for example, intravenous injection, local administration (U.S. Patent 5,328,470) or by stereotactic injection (see, e.g., Chen et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:3054-3057). The pharmaceutical preparation of the
30 gene therapy vector can include the gene therapy vector in an acceptable diluent, or can comprise a slow release matrix in which the gene delivery vehicle is imbedded. Alternatively, where the complete gene delivery vector can be produced intact from recombinant cells, e.g.
35 retroviral vectors, the pharmaceutical preparation can

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include one or more cells which produce the gene delivery system.

The pharmaceutical compositions can be included in a container, pack, or dispenser together with
5 instructions for administration.

V. Uses and Methods of the Invention

The nucleic acid molecules, proteins, protein homologues, and antibodies described herein can be used in one or more of the following methods: a) screening
10 assays; b) detection assays (e.g., chromosomal mapping, tissue typing, forensic biology); c) predictive medicine (e.g., diagnostic assays, prognostic assays, monitoring clinical trials, and pharmacogenomics); and d) methods of treatment (e.g., therapeutic and prophylactic). A
15 Tango-77 protein interacts with other cellular proteins and can thus be used for regulation of inflammation. The polypeptides of the invention can be used in assays to determine biological activity. For example, they could be used in a panel of proteins for high-throughput
20 screening.

The isolated nucleic acid molecules of the invention can be used to express Tango-77 protein (e.g., via a recombinant expression vector in a host cell in gene therapy applications), to detect Tango-77 mRNA
25 (e.g., in a biological sample) or a genetic lesion in a Tango-77 gene, and to modulate Tango-77 activity. In addition, the Tango-77 proteins can be used to screen drugs or compounds which modulate the Tango-77 activity or expression as well as to treat disorders characterized
30 by insufficient or excessive production of Tango-77 protein or production of Tango-77 protein forms which have decreased or aberrant activity compared to Tango-77 wild type protein. In addition, the anti-Tango-77

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antibodies of the invention can be used to detect and isolate Tango-77 proteins and modulate Tango-77 activity.

This invention further pertains to novel agents identified by the above-described screening assays and
5 uses thereof for treatments as described herein.

A. Screening Assays

The invention provides a method (also referred to herein as a "screening assay") for identifying modulators, i.e., candidate or test compounds or agents
10 (e.g., peptides, peptidomimetics, small molecules or other drugs) which bind to Tango-77 proteins or have a stimulatory or inhibitory effect on, for example, Tango-77 expression or Tango-77 activity.

Examples of methods for the synthesis of molecular
15 libraries can be found in the art, for example in:

DeWitt et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:6909;
Erb et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:11422;
Zuckermann et al. (1994). *J. Med. Chem.* 37:2678; Cho et
al. (1993) *Science* 261:1303; Carrell et al. (1994) *Angew.*
20 *Chem. Int. Ed. Engl.* 33:2059; Carell et al. (1994) *Angew.*
Chem. Int. Ed. Engl. 33:2061; and Gallop et al. (1994) *J.*
Med. Chem. 37:1233.

Libraries of compounds may be presented in solution (e.g., Houghten (1992) *Bio/Techniques* 13:412-
25 421), or on beads (Lam (1991) *Nature* 354:82-84), chips (Fodor (1993) *Nature* 364:555-556), bacteria (U.S. Patent No. 5,223,409), spores (Patent Nos. 5,571,698; 5,403,484; and 5,223,409), plasmids (Cull et al. (1992) *Proc. Natl. Acad. Sci. USA* 89:1865-1869) or phage (Scott and Smith
30 (1990) *Science* 249:386-390; Devlin (1990) *Science* 249:404-406; Cwirla et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:6378-6382; and Felici (1991) *J. Mol. Biol.* 222:301-310).

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In another embodiment, an assay is used to determine the ability of the test compound to modulate the activity of Tango-77 or a biologically active portion thereof, for example, by determining the ability of the

5 Tango-77 protein to bind to or interact with a Tango-77 target molecule. As used herein, a "target molecule" is a molecule with which a Tango-77 protein binds or interacts in nature, for example, a molecule on the surface of a cell. A Tango-77 target molecule can be a

10 non-Tango-77 molecule or a Tango-77 protein or polypeptide of the present invention. In one embodiment, a Tango-77 target molecule is a component of a signal transduction pathway, for example, Tango-77 may bind to a IL-1 receptor or another receptor thereby blocking the

15 receptor and inhibiting future signal transduction. Determining the ability of the Tango-77 protein to bind to or interact with a Tango-77 target molecule can be accomplished by one of the methods described above. In a preferred embodiment, determining the ability of the

20 Tango-77 protein to bind to or interact with a Tango-77 target molecule can be accomplished by determining the activity of the target molecule. For example, the activity of the target molecule can be determined by detecting induction of a cellular second messenger of the

25 target (e.g., intracellular Ca^{2+} , diacylglycerol, IP3, etc.), detecting catalytic/enzymatic activity of the target on an appropriate substrate, detecting the induction of a reporter gene (e.g., a Tango-77-responsive regulatory element operably linked to a nucleic acid

30 encoding a detectable marker, e.g. luciferase), or detecting a cellular response, for example, inflammation.

In yet another embodiment, an assay of the present invention is a cell-free assay comprising contacting a Tango-77 protein or biologically active portion thereof

35 with a test compound and determining the ability of the

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test compound to bind to the Tango-77 protein or biologically active portion thereof. Binding of the test compound to the Tango-77 protein can be determined either directly or indirectly as described above. In a
5 preferred embodiment, the assay includes contacting the Tango-77 protein or biologically active portion thereof with a known compound which binds Tango-77 to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test
10 compound to interact with a Tango-77 protein, wherein determining the ability of the test compound to interact with a Tango-77 protein comprises determining the ability of the test compound to preferentially bind to Tango-77 or biologically active portion thereof as compared to the
15 known compound.

In another embodiment, an assay is a cell-free assay comprising contacting Tango-77 protein or biologically active portion thereof with a test compound and determining the ability of the test compound to
20 modulate (e.g., stimulate or inhibit) the activity of the Tango-77 protein or biologically active portion thereof. Determining the ability of the test compound to modulate the activity of Tango-77 can be accomplished, for example, by determining the ability of the Tango-77
25 protein to bind to a Tango-77 target molecule by one of the methods described above for determining direct binding. In an alternative embodiment, determining the ability of the test compound to modulate the activity of Tango-77 can be accomplished by determining the ability
30 of the Tango-77 protein to further modulate a Tango-77 target molecule. For example, the catalytic/enzymatic activity of the target molecule on an appropriate substrate can be determined as previously described.

In yet another embodiment, the cell-free assay
35 comprises contacting the Tango-77 protein or biologically

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active portion thereof with a known compound which binds Tango-77 to form an assay mixture, contacting the assay mixture with a test compound, and determining the ability of the test compound to interact with a Tango-77 protein, wherein determining the ability of the test compound to interact with a Tango-77 protein comprises determining the ability of the Tango-77 protein to preferentially bind to or modulate the activity of a Tango-77 target molecule.

10 It is possible that membrane-bound forms of Tango-77 exist. The cell-free assays of the present invention are amenable to use of both the forms Tango-77. In the case of cell-free assays comprising a membrane-bound form of Tango-77, it may be desirable to utilize a
15 solubilizing agent such that the membrane-bound form of Tango-77 is maintained in solution. Examples of such solubilizing agents include non-ionic detergents such as n-octylglucoside, n-dodecylglucoside, n-dodecylmaltoside, octanoyl-N-methylglucamide, decanoyl-N-methylglucamide,
20 Triton® X-100, Triton® X-114, Thesit®, Isotridecypoly(ethylene glycol ether)n, 3-[(3-cholamidopropyl)dimethylamminio]-1-propane sulfonate (CHAPS), 3-[(3-cholamidopropyl)dimethylamminio]-2-hydroxy-1-propane sulfonate (CHAPSO), or N-dodecyl=N,N-
25 dimethyl-3-ammonio-1-propane sulfonate.

 In more than one embodiment of the above assay methods of the present invention, it may be desirable to immobilize either Tango-77 or its target molecule to facilitate separation of complexed from uncomplexed forms
30 of one or both of the proteins, as well as to accommodate automation of the assay. Binding of a test compound to Tango-77, or interaction of Tango-77 with a target molecule in the presence and absence of a candidate compound, can be accomplished in any vessel suitable for
35 containing the reactants. Examples of such vessels

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include microtitre plates, test tubes, and micro-centrifuge tubes. In one embodiment, a fusion protein can be provided which adds a domain that allows one or both of the proteins to be bound to a matrix. For
5 example, glutathione-S-transferase/ Tango-77 fusion proteins or glutathione-S-transferase/target fusion proteins can be adsorbed onto glutathione sepharose beads (Sigma Chemical Co.; St. Louis, MO) or glutathione derivatized microtitre plates, which are then combined
10 with the test compound or the test compound and either the non-adsorbed target protein or Tango-77 protein, and the mixture incubated under conditions conducive to complex formation (e.g., at physiological conditions for salt and pH). Following incubation, the beads or
15 microtitre plate wells are washed to remove any unbound components and complex formation is measured either directly or indirectly, for example, as described above. Alternatively, the complexes can be dissociated from the matrix, and the level of Tango-77 binding or activity
20 determined using standard techniques.

Other techniques for immobilizing proteins on matrices can also be used in the screening assays of the invention. For example, either Tango-77 or its target molecule can be immobilized utilizing conjugation of
25 biotin and streptavidin. Biotinylated Tango-77 or target molecules can be prepared from biotin-NHS (N-hydroxy-succinimide) using techniques well known in the art (e.g., biotinylation kit, Pierce Chemicals; Rockford, IL), and immobilized in the wells of streptavidin-coated
30 96 well plates (Pierce Chemical). Alternatively, antibodies reactive with Tango-77 or target molecules but which do not interfere with binding of the Tango-77 protein to its target molecule can be derivatized to the wells of the plate, and unbound target or Tango-77
35 trapped in the wells by antibody conjugation. Methods

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for detecting such complexes, in addition to those described above for the GST-immobilized complexes, include immunodetection of complexes using antibodies reactive with the Tango-77 or target molecule, as well as
5 enzyme-linked assays which rely on detecting an enzymatic activity associated with the Tango-77 or target molecule.

In another embodiment, modulators of Tango-77 expression are identified in a method in which a cell is contacted with a candidate compound and the expression of
10 Tango-77 mRNA or protein in the cell is determined. The level of expression of Tango-77 mRNA or protein in the presence of the candidate compound is compared to the level of expression of Tango-77 mRNA or protein in the absence of the candidate compound. The candidate
15 compound can then be identified as a modulator of Tango-77 expression based on this comparison. For example, when expression of Tango-77 mRNA or protein is greater (statistically significantly greater) in the presence of the candidate compound than in its absence,
20 the candidate compound is identified as a stimulator of Tango-77 mRNA or protein expression. Alternatively, when expression of Tango-77 mRNA or protein is less (statistically significantly less) in the presence of the candidate compound than in its absence, the candidate
25 compound is identified as an inhibitor of Tango-77 mRNA or protein expression. The level of Tango-77 mRNA or protein expression in the cells can be determined by methods described herein for detecting Tango-77 mRNA or protein.

30 In yet another aspect of the invention, the Tango-77 proteins can be used as "bait proteins" in a two-hybrid assay or three hybrid assay (see, e.g., U.S. Patent No. 5,283,317; Zervos et al. (1993) *Cell* 72:223-232; Madura et al. (1993) *J. Biol. Chem.* 268:12046-12054;
35 Bartel et al. (1993) *Bio/Techniques* 14:920-924; Iwabuchi

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et al. (1993) *Oncogene* 8:1693-1696; and PCT Publication No. WO 94/10300), to identify other proteins, which bind to or interact with Tango-77 ("Tango-77-binding proteins" or "Tango-77-bp") and modulate Tango-77 activity. Such
5 Tango-77-binding proteins are also likely to be involved in the propagation of signals by the Tango-77 proteins as, for example, upstream or downstream elements of the Tango-77 pathway.

The two-hybrid system is based on the modular
10 nature of most transcription factors, which consist of separable DNA-binding and activation domains. Briefly, the assay utilizes two different DNA constructs. In one construct, the gene that codes for Tango-77 is fused to a gene encoding the DNA binding domain of a known
15 transcription factor (e.g., GAL-4). In the other construct, a DNA sequence, from a library of DNA sequences, that encodes an unidentified protein ("prey" or "sample") is fused to a gene that codes for the activation domain of the known transcription factor. If
20 the "bait" and the "prey" proteins are able to interact, *in vivo*, forming an Tango-77-dependent complex, the DNA-binding and activation domains of the transcription factor are brought into close proximity. This proximity allows transcription of a reporter gene (e.g., LacZ)
25 which is operably linked to a transcriptional regulatory site responsive to the transcription factor. Expression of the reporter gene can be detected and cell colonies containing the functional transcription factor can be isolated and used to obtain the cloned gene which encodes
30 the protein which interacts with Tango-77.

This invention further pertains to novel agents identified by the above-described screening assays and uses thereof for treatments as described herein.

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B. Detection Assays

Portions or fragments of the cDNA sequence identified herein (and the corresponding complete gene sequences) can be used in numerous ways as polynucleotide reagents. For example, the sequence can be used to: (i) map the respective gene on a chromosome and, thus, locate gene regions associated with genetic disease; (ii) identify an individual from a minute biological sample (tissue typing); and (iii) aid in forensic identification of a biological sample. These applications are described in the subsections below.

1. Chromosome Mapping

Once the sequence (or a portion of the sequence) of a gene has been isolated, this sequence can be used to map the location of the gene on a chromosome. Accordingly, Tango-77 nucleic acid molecules described herein or fragments thereof, can be used to map the location of the Tango-77 gene(s) on a chromosome. The mapping of the Tango-77 sequences to chromosomes is an important first step in correlating these sequences with genes associated with disease.

Briefly, a Tango-77 gene can be mapped to chromosomes by preparing PCR primers (preferably 15-25 bp in length) from the Tango-77 sequences. Computer analysis of Tango-77 sequences can be used to rapidly select primers that do not span more than one exon in the genomic DNA, thus complicating the amplification process. These primers can then be used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the Tango-77 sequences will yield an amplified fragment.

Somatic cell hybrids are prepared by fusing somatic cells from different mammals (e.g., human and

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mouse cells). As hybrids of human and mouse cells grow and divide, they gradually lose human chromosomes in random order, but retain the mouse chromosomes. By using media in which mouse cells cannot grow (because they lack a particular enzyme) but in which human cells can, the one human chromosome that contains the gene encoding the needed enzyme, will be retained. By using various media, panels of hybrid cell lines can be established. Each cell line in a panel contains either a single human chromosome or a small number of human chromosomes, and a full set of mouse chromosomes, allowing easy mapping of individual genes to specific human chromosomes. (D'Eustachio et al. (1983) *Science* 220:919-924). Somatic cell hybrids containing only fragments of human chromosomes can also be produced by using human chromosomes with translocations and deletions.

PCR mapping of somatic cell hybrids is a rapid procedure for assigning a particular sequence to a particular chromosome. Three or more sequences can be assigned per day using a single thermal cycler. Using the Tango-77 sequences to design oligonucleotide primers, sublocalization can be achieved with panels of fragments from specific chromosomes. Other mapping strategies which can similarly be used to map a Tango-77 sequence to its chromosome include *in situ* hybridization (described in Fan et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:6223-27), pre-screening with labeled flow-sorted chromosomes, and pre-selection by hybridization to chromosome specific cDNA libraries.

Fluorescence *in situ* hybridization (FISH) of a DNA sequence to a metaphase chromosomal spread can further be used to provide a precise chromosomal location in one step. Chromosome spreads can be made using cells whose division has been blocked in metaphase by a chemical, e.g., colcemid that disrupts the mitotic spindle. The

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chromosomes can be treated briefly with trypsin, and then stained with Giemsa. A pattern of light and dark bands develops on each chromosome, so that the chromosomes can be identified individually. The FISH technique can be
5 used with a DNA sequence as short as 500 or 600 bases. However, clones larger than 1,000 bases have a higher likelihood of binding to a unique chromosomal location with sufficient signal intensity for simple detection. Preferably 1,000 bases, and more preferably 2,000 bases
10 will suffice to get good results at a reasonable amount of time. For a review of this technique, see Verma et al. (Human Chromosomes: A Manual of Basic Techniques (Pergamon Press, New York, 1988)).

Reagents for chromosome mapping can be used
15 individually to mark a single chromosome or a single site on that chromosome, or panels of reagents can be used for marking multiple sites and/or multiple chromosomes. Reagents corresponding to noncoding regions of the genes actually are preferred for mapping purposes. Coding
20 sequences are more likely to be conserved within gene families, thus increasing the chance of cross hybridizations during chromosomal mapping.

Once a sequence has been mapped to a precise chromosomal location, the physical position of the
25 sequence on the chromosome can be correlated with genetic map data. (Such data are found, for example, in V. McKusick, Mendelian Inheritance in Man, available on-line through Johns Hopkins University Welch Medical Library). The relationship between genes and disease, mapped to the
30 same chromosomal region, can then be identified through linkage analysis (co-inheritance of physically adjacent genes), described in, e.g., Egeland et al. (1987) Nature 325:783-787.

Moreover, differences in the DNA sequences between
35 individuals affected and unaffected with a disease

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associated with the Tango-77 gene can be determined. If a mutation is observed in some or all of the affected individuals but not in any unaffected individuals, then the mutation is likely to be the causative agent of the particular disease. Comparison of affected and unaffected individuals generally involves first looking for structural alterations in the chromosomes such as deletions or translocations that are visible from chromosome spreads or detectable using PCR based on that DNA sequence. Ultimately, complete sequencing of genes from several individuals can be performed to confirm the presence of a mutation and to distinguish mutations from polymorphisms.

2. Tissue Typing

The Tango-77 sequences of the present invention can also be used to identify individuals from minute biological samples. The United States military, for example, is considering the use of restriction fragment length polymorphism (RFLP) for identification of its personnel. In this technique, an individual's genomic DNA is digested with one or more restriction enzymes, and probed on a Southern blot to yield unique bands for identification. This method does not suffer from the current limitations of "Dog Tags" which can be lost, switched, or stolen, making positive identification difficult. The sequences of the present invention are useful as additional DNA markers for RFLP (described in U.S. Patent 5,272,057).

Furthermore, the sequences of the present invention can be used to provide an alternative technique which determines the actual base-by-base DNA sequence of selected portions of an individual's genome. Thus, the Tango-77 sequences described herein can be used to prepare two PCR primers from the 5' and 3' ends of the

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sequences. These primers can then be used to amplify an individual's DNA and subsequently sequence it.

Panels of corresponding DNA sequences from individuals, prepared in this manner, can provide unique individual identifications, as each individual will have a unique set of such DNA sequences due to allelic differences. The sequences of the present invention can be used to obtain such identification sequences from individuals and from tissue. The Tango-77 sequences of the invention uniquely represent portions of the human genome. Allelic variation occurs to some degree in the coding regions of these sequences, and to a greater degree in the noncoding regions. It is estimated that allelic variation between individual humans occurs with a frequency of about once per each 500 bases. Each of the sequences described herein can, to some degree, be used as a standard against which DNA from an individual can be compared for identification purposes. Because greater numbers of polymorphisms occur in the noncoding regions, fewer sequences are necessary to differentiate individuals. The noncoding sequences of SEQ ID NO:1 can comfortably provide positive individual identification with a panel of perhaps 10 to 1,000 primers which each yield a noncoding amplified sequence of 100 bases. If predicted coding sequences, such as those in SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10 are used, a more appropriate number of primers for positive individual identification would be 500-2,000.

If a panel of reagents from Tango-77 sequences described herein is used to generate a unique identification database for an individual, those same reagents can later be used to identify tissue from that individual. Using the unique identification database, positive identification of the individual, living or dead, can be made from extremely small tissue samples.

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3. Use of Partial Tango-77 Sequences in Forensic Biology

DNA-based identification techniques can also be used in forensic biology. Forensic biology is a scientific field employing genetic typing of biological evidence found at a crime scene as a means for positively identifying, for example, a perpetrator of a crime. To make such an identification, PCR technology can be used to amplify DNA sequences taken from very small biological samples such as tissues, e.g., hair or skin, or body fluids, e.g., blood, saliva, or semen found at a crime scene. The amplified sequence can then be compared to a standard, thereby allowing identification of the origin of the biological sample.

The sequences of the present invention can be used to provide polynucleotide reagents, e.g., PCR primers, targeted to specific loci in the human genome, which can enhance the reliability of DNA-based forensic identifications by, for example, providing another "identification marker" (i.e. another DNA sequence that is unique to a particular individual). As mentioned above, actual base sequence information can be used for identification as an accurate alternative to patterns formed by restriction enzyme generated fragments. Sequences targeted to noncoding regions of SEQ ID NO:1 are particularly appropriate for this use as greater numbers of polymorphisms occur in the noncoding regions, making it easier to differentiate individuals using this technique. Examples of polynucleotide reagents include the Tango-77 sequences or portions thereof, e.g., fragments derived from the noncoding regions of SEQ ID NO:1 having a length of at least 20 or 30 bases.

The Tango-77 sequences described herein can further be used to provide polynucleotide reagents, e.g., labeled or labelable probes which can be used in, for

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example, an *in situ* hybridization technique, to identify a specific tissue, e.g., brain tissue. This can be very useful in cases where a forensic pathologist is presented with a tissue of unknown origin. Panels of such Tango-77 probes can be used to identify tissue by species and/or by organ type.

In a similar fashion, these reagents, e.g., Tango-77 primers or probes can be used to screen tissue culture for contamination (i.e., screen for the presence of a mixture of different types of cells in a culture).

C. Predictive Medicine

The present invention also pertains to the field of predictive medicine in which diagnostic assays, prognostic assays, pharmacogenomics, and monitoring clinical trails are used for prognostic (predictive) purposes to thereby treat an individual prophylactically. Accordingly, one aspect of the present invention relates to diagnostic assays for determining Tango-77 protein and/or nucleic acid expression as well as Tango-77 activity, in the context of a biological sample (e.g., blood, serum, cells, tissue) to thereby determine whether an individual is afflicted with a disease or disorder, or is at risk of developing a disorder, associated with aberrant Tango-77 expression or activity. The invention also provides for prognostic (or predictive) assays for determining whether an individual is at risk of developing a disorder associated with Tango-77 protein, nucleic acid expression or activity. For example, mutations in a Tango-77 gene can be assayed in a biological sample. Such assays can be used for prognostic or predictive purpose to thereby prophylactically treat an individual prior to the onset of a disorder characterized by or associated with Tango-77 protein, nucleic acid expression or activity.

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Another aspect of the invention provides methods for determining Tango-77 protein, nucleic acid expression or Tango-77 activity in an individual to thereby select appropriate therapeutic or prophylactic agents for that individual (referred to herein as "pharmacogenomics"). Pharmacogenomics allows for the selection of agents (e.g., drugs) for therapeutic or prophylactic treatment of an individual based on the genotype of the individual (e.g., the genotype of the individual examined to determine the ability of the individual to respond to a particular agent.)

Yet another aspect of the invention pertains to monitoring the influence of agents (e.g., drugs or other compounds) on the expression or activity of Tango-77 in clinical trials.

These and other agents are described in further detail in the following sections.

1. Diagnostic Assays

An exemplary method for detecting the presence or absence of Tango-77 in a biological sample involves obtaining a biological sample from a test subject and contacting the biological sample with a compound or an agent capable of detecting Tango-77 protein or nucleic acid (e.g., mRNA, genomic DNA) that encodes Tango-77 protein such that the presence of Tango-77 is detected in the biological sample. A preferred agent for detecting Tango-77 mRNA or genomic DNA is a labeled nucleic acid probe capable of hybridizing to Tango-77 mRNA or genomic DNA. The nucleic acid probe can be, for example, a full-length Tango-77 nucleic acid, such as the nucleic acid of SEQ ID NO: 1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or a portion thereof, such as an oligonucleotide of at least 15, 30, 50, 100, 250 or 500 nucleotides in length and sufficient to specifically hybridize under stringent

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conditions to Tango-77 mRNA or genomic DNA. Other suitable probes for use in the diagnostic assays of the invention are described herein.

A preferred agent for detecting Tango-77 protein is an antibody capable of binding to Tango-77 protein, preferably an antibody with a detectable label. Antibodies can be polyclonal, or more preferably, monoclonal. An intact antibody, or a fragment thereof (e.g., Fab or F(ab')₂) can be used. The term "labeled", with regard to the probe or antibody, is intended to encompass direct labeling of the probe or antibody by coupling (i.e., physically linking) a detectable substance to the probe or antibody, as well as indirect labeling of the probe or antibody by reactivity with another reagent that is directly labeled. Examples of indirect labeling include detection of a primary antibody using a fluorescently labeled secondary antibody and end-labeling of a DNA probe with biotin such that it can be detected with fluorescently labeled streptavidin. The term "biological sample" is intended to include tissues, cells and biological fluids isolated from a subject, as well as tissues, cells and fluids present within a subject. That is, the detection method of the invention can be used to detect Tango-77 mRNA, protein, or genomic DNA in a biological sample *in vitro* as well as *in vivo*. For example, *in vitro* techniques for detection of Tango-77 mRNA include Northern hybridizations and *in situ* hybridizations. *In vitro* techniques for detection of Tango-77 protein include enzyme linked immunosorbent assays (ELISAs), Western blots, immunoprecipitations and immunofluorescence. *In vitro* techniques for detection of Tango-77 genomic DNA include Southern hybridizations. Furthermore, *in vivo* techniques for detection of Tango-77 protein include introducing into a subject a labeled anti-Tango-77 antibody. For example, the antibody can be

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labeled with a radioactive marker whose presence and location in a subject can be detected by standard imaging techniques.

In one embodiment, the biological sample contains
5 protein molecules from the test subject. Alternatively,
the biological sample can contain mRNA molecules from the
test subject or genomic DNA molecules from the test
subject. A preferred biological sample is a peripheral
blood leukocyte sample isolated by conventional means
10 from a subject.

In another embodiment, the methods further involve
obtaining a control biological sample from a control
subject, contacting the control sample with a compound or
agent capable of detecting Tango-77 protein, mRNA, or
15 genomic DNA, such that the presence of Tango-77 protein,
mRNA or genomic DNA is detected in the biological sample,
and comparing the presence of Tango-77 protein, mRNA or
genomic DNA in the control sample with the presence of
Tango-77 protein, mRNA or genomic DNA in the test sample.

20 The invention also encompasses kits for detecting
the presence of Tango-77 in a biological sample (a test
sample). Such kits can be used to determine if a subject
is suffering from or is at increased risk of developing a
disorder associated with aberrant expression of Tango-77
25 (e.g., an immunological disorder). For example, the kit
can comprise a labeled compound or agent capable of
detecting Tango-77 protein or mRNA in a biological sample
and means for determining the amount of Tango-77 in the
sample (e.g., an anti-Tango-77 antibody or an
30 oligonucleotide probe which binds to DNA encoding
Tango-77, e.g., SEQ ID NO:1 or SEQ ID NO:3 or SEQ ID
NO:6, or SEQ ID NO:10). Kits may also include
instruction for observing that the tested subject is
suffering from or is at risk of developing a disorder
35 associated with aberrant expression of Tango-77 if the

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amount of Tango-77 protein or mRNA is above or below a normal level.

For antibody-based kits, the kit may comprise, for example: (1) a first antibody (e.g., attached to a solid support) which binds to Tango-77 protein; and, optionally (2) a second, different antibody which binds to Tango-77 protein or the first antibody and is conjugated to a detectable agent.

For oligonucleotide-based kits, the kit may comprise, for example: (1) an oligonucleotide, e.g., a detectably labelled oligonucleotide, which hybridizes to a Tango-77 nucleic acid sequence or (2) a pair of primers useful for amplifying a Tango-77 nucleic acid molecule;

The kit may also comprise, e.g., a buffering agent, a preservative, or a protein stabilizing agent. The kit may also comprise components necessary for detecting the detectable agent (e.g., an enzyme or a substrate). The kit may also contain a control sample or a series of control samples which can be assayed and compared to the test sample contained. Each component of the kit is usually enclosed within an individual container and all of the various containers are within a single package along with instructions for observing whether the tested subject is suffering from or is at risk of developing a disorder associated with aberrant expression of Tango-77.

2. Prognostic Assays

The methods described herein can furthermore be utilized as diagnostic or prognostic assays to identify subjects having or at risk of developing a disease or disorder associated with aberrant Tango-77 expression or activity. For example, the assays described herein, such as the preceding diagnostic assays or the following assays, can be utilized to identify a subject having or

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at risk of developing a disorder associated with aberrant expression or activity. Thus, the present invention provides a method in which a test sample is obtained from a subject and Tango-77 protein or nucleic acid (e.g., mRNA, genomic DNA) is detected, wherein the presence of Tango-77 protein or nucleic acid is diagnostic for a subject having or at risk of developing a disease or disorder associated with aberrant Tango-77 expression or activity. As used herein, a "test sample" refers to a biological sample obtained from a subject of interest. For example, a test sample can be a biological fluid (e.g., serum), cell sample, or tissue.

Furthermore, the prognostic assays described herein can be used to determine whether a subject can be administered an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate) to treat a disease or disorder associated with aberrant Tango-77 expression or activity. For example, such methods can be used to determine whether a subject can be effectively treated with a specific agent or class of agents (e.g., agents of a type which decrease Tango-77 activity). Thus, the present invention provides methods for determining whether a subject can be effectively treated with an agent for a disorder associated with aberrant Tango-77 expression or activity in which a test sample is obtained and Tango-77 protein or nucleic acid is detected (e.g., wherein the presence of Tango-77 protein or nucleic acid is diagnostic for a subject that can be administered the agent to treat a disorder associated with aberrant Tango-77 expression or activity).

The methods of the invention can also be used to detect genetic lesions or mutations in a Tango-77 gene, thereby determining if a subject with the lesioned gene is at risk for a disorder characterized by aberrant

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inflammation. In preferred embodiments, the methods include detecting, in a sample of cells from the subject, the presence or absence of a genetic lesion or mutation characterized by at least one of an alteration affecting
5 the integrity of a gene encoding a Tango-77-protein, or the mis-expression of the Tango-77 gene. For example, such genetic lesions or mutations can be detected by ascertaining the existence of at least one of: 1) a deletion of one or more nucleotides from a Tango-77 gene;
10 2) an addition of one or more nucleotides to a Tango-77 gene; 3) a substitution of one or more nucleotides of a Tango-77 gene; 4) a chromosomal rearrangement of a Tango-77 gene; 5) an alteration in the level of a messenger RNA transcript of a Tango-77 gene; 6) an
15 aberrant modification of a Tango-77 gene, such as of the methylation pattern of the genomic DNA; 7) the presence of a non-wild type splicing pattern of a messenger RNA transcript of a Tango-77 gene; 8) a non-wild type level of a Tango-77-protein; 9) an allelic loss of a Tango-77
20 gene, and 10) an inappropriate post-translational modification of a Tango-77-protein. As described herein, there are a large number of assay techniques known in the art which can be used for detecting lesions or mutations in a Tango-77 gene. A preferred biological sample is a
25 peripheral blood leukocyte sample isolated by conventional means from a subject.

In certain embodiments, detection of the lesion involves the use of a probe/primer in a polymerase chain reaction (PCR) (see, e.g., U.S. Patent Nos. 4,683,195 and
30 4,683,202), such as anchor PCR or RACE PCR, or, alternatively, in a ligation chain reaction (LCR) (see, e.g., Landegran et al. (1988) *Science* 241:1077-1080; and Nakazawa et al. (1994) *Proc. Natl. Acad. Sci. USA* 91:360-364), the latter of which can be particularly useful for
35 detecting point mutations in the Tango-77-gene (see,

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e.g., Abravaya et al. (1995) *Nucleic Acids Res.* 23:675-682). This method can include the steps of collecting a sample of cells from a patient, isolating nucleic acid (e.g., genomic, mRNA or both) from the cells of the
5 sample, contacting the nucleic acid sample with one or more primers which specifically hybridize to a Tango-77 gene under conditions such that hybridization and amplification of the Tango-77-gene (if present) occurs, and detecting the presence or absence of an amplification
10 product, or detecting the size of the amplification product and comparing the length to a control sample. It is anticipated that PCR and/or LCR may be desirable to use as a preliminary amplification step in conjunction with any of the techniques used for detecting mutations
15 described herein.

Alternative amplification methods include: self sustained sequence replication (Guatelli et al. (1990) *Proc. Natl. Acad. Sci. USA* 87:1874-1878), transcriptional amplification system (Kwoh, et al. (1989) *Proc. Natl.*
20 *Acad. Sci. USA* 86:1173-1177), Q-Beta Replicase (Lizardi et al. (1988) *Bio/Technology* 6:1197), or any other nucleic acid amplification method, followed by the detection of the amplified molecules using techniques well known to those of skill in the art. These detection
25 schemes are especially useful for the detection of nucleic acid molecules if such molecules are present in very low numbers.

In an alternative embodiment, mutations in a Tango-77 gene from a sample cell can be identified by
30 alterations in restriction enzyme cleavage patterns. For example, sample and control DNA is isolated, amplified (optionally), digested with one or more restriction endonucleases, and fragment length sizes are determined by gel electrophoresis and compared. Differences in
35 fragment length sizes between sample and control DNA

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indicates mutations in the sample DNA. Moreover, the use of sequence specific ribozymes (see, e.g., U.S. Patent No. 5,498,531) can be used to score for the presence of specific mutations by development or loss of a ribozyme cleavage site.

In other embodiments, genetic mutations in Tango-77 can be identified by hybridizing a sample and control nucleic acids, e.g., DNA or RNA, to high density arrays containing hundreds or thousands of oligonucleotide probes (Cronin et al. (1996) *Human Mutation* 7:244-255; Kozal et al. (1996) *Nature Medicine* 2:753-759). For example, genetic mutations in Tango-77 can be identified in two-dimensional arrays containing light-generated DNA probes as described in Cronin et al. supra. Briefly, a first hybridization array of probes can be used to scan through long stretches of DNA in a sample and control to identify base changes between the sequences by making linear arrays of sequential overlapping probes. This step allows the identification of point mutations. This step is followed by a second hybridization array that allows the characterization of specific mutations by using smaller, specialized probe arrays complementary to all variants or mutations detected. Each mutation array is composed of parallel probe sets, one complementary to the wild-type gene and the other complementary to the mutant gene.

In yet another embodiment, any of a variety of sequencing reactions known in the art can be used to directly sequence the Tango-77 gene and detect mutations by comparing the sequence of the sample Tango-77 with the corresponding wild-type (control) sequence. Examples of sequencing reactions include those based on techniques developed by Maxim and Gilbert ((1977) *Proc. Natl. Acad. Sci. USA* 74:560) or Sanger ((1977) *Proc. Natl. Acad. Sci. USA* 74:5463). It is also contemplated that any of a

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variety of automated sequencing procedures can be utilized when performing the diagnostic assays ((1995) *Bio/Techniques* 19:448), including sequencing by mass spectrometry (see, e.g., PCT Publication No. WO 94/16101; 5 Cohen et al. (1996) *Adv. Chromatogr.* 36:127-162; and Griffin et al. (1993) *Appl. Biochem. Biotechnol.* 38:147-159).

Other methods for detecting mutations in the Tango-77 gene include methods in which protection from 10 cleavage agents is used to detect mismatched bases in RNA/RNA or RNA/DNA heteroduplexes (Myers et al. (1985) *Science* 230:1242). In general, the technique of "mismatch cleavage" entails providing heteroduplexes formed by hybridizing (labeled) RNA or DNA containing the 15 wild-type Tango-77 sequence with potentially mutant RNA or DNA obtained from a tissue sample. The double-stranded duplexes are treated with an agent which cleaves single-stranded regions of the duplex such as which will exist due to basepair mismatches between the control and 20 sample strands. RNA/DNA duplexes can be treated with RNase to digest mismatched regions, and DNA/DNA hybrids can be treated with S1 nuclease to digest mismatched regions. In other embodiments, either DNA/DNA or RNA/DNA duplexes can be treated with hydroxylamine or osmium 25 tetroxide and with piperidine in order to digest mismatched regions. After digestion of the mismatched regions, the resulting material is then separated by size on denaturing polyacrylamide gels to determine the site of mutation. See, e.g., Cotton et al. (1988) *Proc. Natl. Acad. Sci. USA* 85:4397; Saleeba et al. (1992) *Methods Enzymol.* 217:286-295. In a preferred embodiment, the 30 control DNA or RNA can be labeled for detection.

In still another embodiment, the mismatch cleavage reaction employs one or more proteins that recognize 35 mismatched base pairs in double-stranded DNA (so called

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"DNA mismatch repair" enzymes) in defined systems for detecting and mapping point mutations in Tango-77 cDNAs obtained from samples of cells. For example, the mutY enzyme of *E. coli* cleaves A at G/A mismatches and the
5 thymidine DNA glycosylase from HeLa cells cleaves T at G/T mismatches (Hsu et al. (1994) *Carcinogenesis* 15:1657-1662). According to an exemplary embodiment, a probe based on a Tango-77 sequence, e.g., a wild-type Tango-77 sequence, is hybridized to a cDNA or other DNA product
10 from a test cell(s). The duplex is treated with a DNA mismatch repair enzyme, and the cleavage products, if any, can be detected from electrophoresis protocols or the like. See, e.g., U.S. Patent No. 5,459,039.

In other embodiments, alterations in
15 electrophoretic mobility will be used to identify mutations in Tango-77 genes. For example, single strand conformation polymorphism (SSCP) may be used to detect differences in electrophoretic mobility between mutant and wild type nucleic acids (Orita et al. (1989) *Proc.*
20 *Natl. Acad. Sci. USA* 86:2766; see also Cotton (1993) *Mutat. Res.* 285:125-144; Hayashi (1992) *Genet Anal Tech Appl* 9:73-79). Single-stranded DNA fragments of sample and control Tango-77 nucleic acids will be denatured and allowed to renature. The secondary structure of single-
25 stranded nucleic acids varies according to sequence, and the resulting alteration in electrophoretic mobility enables the detection of even a single base change. The DNA fragments may be labeled or detected with labeled probes. The sensitivity of the assay may be enhanced by
30 using RNA (rather than DNA), in which the secondary structure is more sensitive to a change in sequence. In a preferred embodiment, the subject method utilizes heteroduplex analysis to separate double stranded heteroduplex molecules on the basis of changes in

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electrophoretic mobility (Keen et al. (1991) *Trends Genet* 7:5).

In yet another embodiment, the movement of mutant or wild-type fragments in polyacrylamide gels containing
5 a gradient of denaturant is assayed using denaturing gradient gel electrophoresis (DGGE) (Myers et al. (1985) *Nature* 313:495). When DGGE is used as the method of analysis, DNA will be modified to insure that it does not completely denature, for example by adding a GC clamp of
10 approximately 40 bp of high-melting GC-rich DNA by PCR. In a further embodiment, a temperature gradient is used in place of a denaturing gradient to identify differences in the mobility of control and sample DNA (Rosenbaum and Reissner (1987) *Biophys. Chem.* 265:12753).

15 Examples of other techniques for detecting point mutations include, but are not limited to, selective oligonucleotide hybridization, selective amplification, or selective primer extension. For example, oligonucleotide primers may be prepared in which the
20 known mutation is placed centrally and then hybridized to target DNA under conditions which permit hybridization only if a perfect match is found (Saiki et al. (1986) *Nature* 324:163); Saiki et al. (1989) *Proc. Natl. Acad. Sci. USA* 86:6230). Such allele specific oligonucleotides
25 are hybridized to PCR amplified target DNA or a number of different mutations when the oligonucleotides are attached to the hybridizing membrane and hybridized with labeled target DNA.

Alternatively, allele specific amplification
30 technology which depends on selective PCR amplification may be used in conjunction with the instant invention. Oligonucleotides used as primers for specific amplification may carry the mutation of interest in the center of the molecule (so that amplification depends on
35 differential hybridization) (Gibbs et al. (1989) *Nucleic*

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Acids Res. 17:2437-2448) or at the extreme 3' end of one primer where, under appropriate conditions, mismatch can prevent or reduce polymerase extension (Prossner (1993) *Tibtech* 11:238). In addition, it may be desirable to
5 introduce a novel restriction site in the region of the mutation to create cleavage-based detection (Gasparini et al. (1992) *Mol. Cell Probes* 6:1). It is anticipated that in certain embodiments amplification may also be performed using Taq ligase for amplification (Barany
10 (1991) *Proc. Natl. Acad. Sci USA* 88:189). In such cases, ligation will occur only if there is a perfect match at the 3' end of the 5' sequence making it possible to detect the presence of a known mutation at a specific site by looking for the presence or absence of
15 amplification.

The methods described herein may be performed, for example, by utilizing pre-packaged diagnostic kits comprising at least one probe nucleic acid or antibody reagent described herein, which may be conveniently used,
20 e.g., in clinical settings to diagnose patients exhibiting symptoms or family history of a disease or illness involving a Tango-77 gene.

Furthermore, any cell type or tissue, preferably peripheral blood leukocytes, in which Tango-77 is
25 expressed may be utilized in the prognostic assays described herein.

3. Pharmacogenomics

Agents, or modulators which have a stimulatory or
30 inhibitory effect on Tango-77 activity (e.g., Tango-77 gene expression) as identified by a screening assay described herein can be administered to individuals to treat (prophylactically or therapeutically) disorders (e.g., acute or chronic inflammation and asthma)
35 associated with aberrant Tango-77 activity. In

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conjunction with such treatment, the pharmacogenomics (i.e., the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of the individual may be considered. Differences in metabolism of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual permits the selection of effective agents (e.g., drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens. Accordingly, the activity of Tango-77 protein, expression of Tango-77 nucleic acid, or mutation content of Tango-77 genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons. See, e.g., Linder (1997) *Clin. Chem.* 43(2):254-266. In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body are referred to as "altered drug action." Genetic conditions transmitted as single factors altering the way the body acts on drugs are referred to as "altered drug metabolism". These pharmacogenetic conditions can occur either as rare defects or as polymorphisms. For example, glucose-6-phosphate dehydrogenase deficiency (G6PD) is a common inherited enzymopathy in which the main clinical complication is haemolysis after ingestion of oxidant drugs (anti-

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malarials, sulfonamides, analgesics, nitrofurans) and consumption of fava beans.

As an illustrative embodiment, the activity of drug metabolizing enzymes is a major determinant of both the intensity and duration of drug action. The discovery of genetic polymorphisms of drug metabolizing enzymes (e.g., N-acetyltransferase 2 (NAT 2) and cytochrome P450 enzymes CYP2D6 and CYP2C19) has provided an explanation as to why some patients do not obtain the expected drug effects or show exaggerated drug response and serious toxicity after taking the standard and safe dose of a drug. These polymorphisms are expressed in two phenotypes in the population, the extensive metabolizer (EM) and poor metabolizer (PM). The prevalence of PM is different among different populations. For example, the gene coding for CYP2D6 is highly polymorphic and several mutations have been identified in PM, which all lead to the absence of functional CYP2D6. Poor metabolizers of CYP2D6 and CYP2C19 quite frequently experience exaggerated drug response and side effects when they receive standard doses. If a metabolite is the active therapeutic moiety, PM shows no therapeutic response, as demonstrated for the analgesic effect of codeine mediated by its CYP2D6-formed metabolite morphine. The other extreme are the so called ultra-rapid metabolizers who do not respond to standard doses. Recently, the molecular basis of ultra-rapid metabolism has been identified to be due to CYP2D6 gene amplification.

Thus, the activity of Tango-77 protein, expression of Tango-77 nucleic acid, or mutation content of Tango-77 genes in an individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual. In addition, pharmacogenetic studies can be used to apply genotyping of polymorphic alleles encoding drug-metabolizing enzymes

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to the identification of an individual's drug responsiveness phenotype. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when treating a subject with a Tango-77 modulator, such as a modulator identified by one of the exemplary screening assays described herein.

4. Monitoring of Effects During Clinical Trials

Monitoring the influence of agents (e.g., drugs, compounds) on the expression or activity of Tango-77 (e.g., the ability to modulate aberrant inflammation) can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent, as determined by a screening assay as described herein, to increase Tango-77 gene expression, increase protein levels, or upregulate Tango-77 activity, can be monitored in clinical trials of subjects exhibiting decreased Tango-77 gene expression, decreased protein levels, or downregulated Tango-77 activity. Alternatively, the effectiveness of an agent, as determined by a screening assay, to decrease Tango-77 gene expression, decrease protein levels, or downregulate Tango-77 activity, can be monitored in clinical trials of subjects exhibiting increased Tango-77 gene expression, increased protein levels, or upregulated Tango-77 activity.

For example, and not by way of limitation, genes, including Tango-77, that are modulated in cells by treatment with an agent (e.g., compound, drug or small molecule) which modulates Tango-77 activity (e.g., as identified in a screening assay described herein) can be identified. Thus, to study the effect of agents on cellular proliferation disorders, for example, in a clinical trial, cells can be isolated and RNA prepared

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and analyzed for the levels of expression of Tango-77 and other genes implicated in the disorder. The levels of gene expression (i.e., a gene expression pattern) can be quantified by Northern blot analysis or RT-PCR, as described herein, or alternatively by measuring the amount of protein produced, by one of the methods as described herein, or by measuring the levels of activity of Tango-77 or other genes. In this way, the gene expression pattern can serve as a marker, indicative of the physiological response of the cells to the agent. Accordingly, this response state may be determined before, and at various points during, treatment of the individual with the agent.

In a preferred embodiment, the present invention provides a method for monitoring the effectiveness of treatment of a subject with an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate identified by the screening assays described herein) comprising the steps of (i) obtaining a pre-administration sample from a subject prior to administration of the agent; (ii) detecting the level of expression of a Tango-77 protein, mRNA, or genomic DNA in the preadministration sample; (iii) obtaining one or more post-administration samples from the subject; (iv) detecting the level of expression or activity of the Tango-77 protein, mRNA, or genomic DNA in the post-administration samples; (v) comparing the level of expression or activity of the Tango-77 protein, mRNA, or genomic DNA in the pre-administration sample with the Tango-77 protein, mRNA, or genomic DNA in the post administration sample or samples; and (vi) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be desirable to increase the expression or activity of Tango-77 to higher levels than detected,

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i.e., to increase the effectiveness of the agent. Alternatively, decreased administration of the agent may be desirable to decrease expression or activity of Tango-77 to lower levels than detected, i.e., to decrease
5 the effectiveness of the agent.

C. Methods of Treatment

The present invention provides for both prophylactic and therapeutic methods of treating a subject at risk of (or susceptible to) developing or
10 having a disorder associated with aberrant Tango-77 expression or activity. Alternatively, disorders associated with aberrant IL-1 production can be treated with Tango-77. Such disorders include acute and chronic inflammation, asthma, some classes of arthritis,
15 autoimmune diabetes, systemic lupus erythematosus and inflammatory bowel disease.

1. Prophylactic Methods

In one aspect, the invention provides a method for preventing in a subject, a disease or condition
20 associated with an aberrant Tango-77 expression or activity (or aberrant IL-1 expression or activity), by administering to the subject an agent which modulates Tango-77 expression or at least one Tango-77 activity. Subjects at risk for a disease which is caused or
25 contributed to by aberrant Tango-77 expression or activity can be identified by, for example, any or a combination of diagnostic or prognostic assays as described herein. Administration of a prophylactic agent can occur prior to the manifestation of symptoms
30 characteristic of the Tango-77 aberrancy, such that a disease or disorder is prevented or, alternatively, delayed in its progression. Depending on the type of Tango-77 aberrancy, for example, a Tango-77 agonist or Tango-77 antagonist agent can be used for treating the

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subject. The appropriate agent can be determined based on screening assays described herein.

2. Therapeutic Methods

Another aspect of the invention pertains to
5 methods of modulating Tango-77 expression or activity for
therapeutic purposes. The modulatory method of the
invention involves contacting a cell with an agent that
modulates one or more of the activities of Tango-77
protein activity associated with the cell. An agent that
10 modulates Tango-77 protein activity can be an agent as
described herein, such as a nucleic acid or a protein, a
naturally-occurring cognate ligand of a Tango-77 protein,
a peptide, a Tango-77 peptidomimetic, or other small
molecule. In one embodiment, the agent stimulates one or
15 more of the biological activities of Tango-77 protein.
Examples of such stimulatory agents include active
Tango-77 protein and a nucleic acid molecule encoding
Tango-77 that has been introduced into the cell. In
another embodiment, the agent inhibits one or more of the
20 biological activities of Tango-77 protein. Examples of
such inhibitory agents include antisense Tango-77 nucleic
acid molecules and anti-Tango-77 antibodies. These
modulatory methods can be performed *in vitro* (e.g., by
culturing the cell with the agent) or, alternatively, *in*
25 *vivo* (e.g, by administering the agent to a subject). As
such, the present invention provides methods of treating
an individual afflicted with a disease or disorder
characterized by aberrant expression or activity of a
Tango-77 protein or nucleic acid molecule. In one
30 embodiment, the method involves administering an agent
(e.g., an agent identified by a screening assay described
herein), or combination of agents that modulates (e.g.,
upregulates or downregulates) Tango-77 expression or
activity. In another embodiment, the method involves

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administering a Tango-77 protein or nucleic acid molecule as therapy to compensate for reduced or aberrant Tango-77 expression or activity.

Stimulation of Tango-77 activity is desirable in situations in which Tango-77 is abnormally downregulated and/or in which increased Tango-77 activity is likely to have a beneficial effect. Conversely, inhibition of Tango-77 activity is desirable in situations in which Tango-77 is abnormally upregulated and/or in which decreased Tango-77 activity is likely to have a beneficial effect.

This invention is further illustrated by the following examples which should not be construed as limiting. The contents of all references, patents and published patent applications cited throughout this application are hereby incorporated by reference.

EXAMPLES

Example 1: Isolation and Characterization of Human Tango-77 cDNAs

Cytokine genes IL-1 α , IL-1 β and IL-1ra have been found to be closely clustered on chromosome 2, i.e., IL-1 α , IL-1 β and IL-1ra are located within 450 kb of each other. BAC clones containing IL-1 α and IL-1 β were used to identify other proximal unknown cytokine genes. To do this, a BAC clone containing IL-1 α and IL-1 β was selected from a BAC library (Research Genetics, Huntsville, Alabama) using specific primers designed against IL-1 α and IL-1 β . The DNA from the BAC was extracted and used to make a random-sheared genomic library. From this BAC library, 4000 clones were selected for sequencing. The resulting genomic sequences were then assembled into contigs and used to screen proprietary and public data bases. One genomic contig was found to contain two

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segments of sequences which resemble IL-1ra. These two segments are potential exons of Tango-77 gene.

Two PCR primers were then designed from the two potential exons and used to screen a panel of cDNA
5 libraries for the expression of a Tango-77 message. A cDNA library from TNF- α treated human lung epithelia showed a positive band of the predicted size (i.e., if the two exons are spliced together). Using the PCR fragment as a probe, a single cDNA clone was isolated
10 from the same library. This cDNA contains an insert of 989 bp. The cDNA clone contains three possible open reading frames. The first open reading frame encompasses 534 nucleotides (nucleotides 356-889 of SEQ ID NO:1; SEQ ID NO:3) and encodes a 178 amino acid protein (SEQ ID
15 NO:2). This protein may include a predicted signal sequence of about 63 amino acids (from amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID NO:4)) and a predicted mature protein of about 115 amino acids (from about amino acid 64 to amino acid 178 of SEQ ID NO:2 (SEQ
20 ID NO:5)).

The second putative nucleotide open reading frame encompasses 498 nucleotides (nucleotides 389-889 of SEQ ID NO:1; SEQ ID NO:6) and encodes a 167 amino acid protein (SEQ ID NO:7). This protein includes a predicted
25 signal sequence of about 52 amino acids (from amino acid 1 to about amino acid 52 of SEQ ID NO:7 (SEQ ID NO:8)) and a predicted mature protein of about 115 amino acids (from about amino acid 53 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:9)).

30 The third open reading frame (nucleotides 372-889 of SEQ ID NO:1; SEQ ID NO:10) encompasses 408 nucleotides and encodes a 136 amino acid protein (SEQ ID NO:11). This protein includes a predicted signal sequence of about 21 amino acids (from amino acid 1 to about amino
35 acid 21 of SEQ ID NO:11 (SEQ ID NO:12)) and a predicted

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mature protein of about 115 amino acids (from about amino acid 22 to amino acid 136 of SEQ ID NO:11 (SEQ ID NO:13)).

Tango-77 is predicted to be 35% identical to human IL-1ra at the amino acid level.

Example 2: Expression of Tango-77 mRNA in Human Tissues

The expression of Tango-77 was analyzed using Northern blot hybridization. A PCR generated 989 bp Tango-77 product was radioactively labeled with ³²P-dCTP using the Prime-It kit (Stratagene; La Jolla, CA) according to the instructions of the supplier. Filters containing human mRNA (MTNI and MTNII: Clontech; Palo Alto, CA) were probed in ExpressHyb hybridization solution (Clontech) and washed at high stringency according to manufacturer's recommendations.

Tango-77 mRNA was not detected in any unstimulated tissues (brain, liver, spleen, skeletal muscle, testis, pancreas, heart, kidney and peripheral blood leukocytes) mRNA on Clontech Northern blots.

Over 96 cDNA libraries were then tested for the presence of Tango-77 using PCR amplification. Only three libraries displayed a positive signal. These libraries were the TNF α -treated bronchoepithelium, TNF α -treated SSC cell line and anti-CD3-treated T cells.

Example 3: Characterization of Tango-77 Proteins

In this example, the predicted amino acid sequence of human Tango-77 protein was compared to the amino acid sequence of known protein IL-1ra. In addition, the molecular weight of the human Tango-77 proteins was predicted.

The human Tango-77 cDNA (Figure 1; SEQ ID NO:1) isolated as described above encodes a 178 amino acid protein (Figure 1; SEQ ID NO:2) or a 167 amino acid

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protein (Figure 1; SEQ ID NO:7) or a 136 amino acid protein (Figure 1; SEQ ID NO:11). The signal peptide prediction program SIGNALP Optimized Tool (Nielsen et al. (1997) *Protein Engineering* 10:1-6) predicted that

5 Tango-77 includes a 63 amino acid signal peptide (amino acid 1 to about amino acid 63 of SEQ ID NO:2 (SEQ ID NO:4)) preceding the 115 mature protein; or preceding the 115 mature protein (about amino acid 52 to amino acid 167 of SEQ ID NO:7 (SEQ ID NO:8)); or preceding the 115

10 mature protein (about amino acid 21 to amino acid 136 of SEQ ID NO:11;SEQ ID NO:12).

As shown in Figure 2, Tango-77 has a region of homology to IL-1ra (SEQ ID NO:14).

Mature Tango-77 has a predicted MW of about 13 kDa

15 and the predicted MW for the immature Tango-77 is 19.6 kDa, 18.5 kDa or 15.2 kDa, not including post-translational modifications.

Example 4: Preparation of Tango-77 Proteins

Recombinant Tango-77 can be produced in a variety

20 of expression systems. For example, the mature Tango-77 peptide can be expressed as a recombinant glutathione-S-transferase (GST) fusion protein in *E. coli* and the fusion protein can be isolated and characterized. Specifically, as described above, Tango-77 can be fused

25 to GST and this fusion protein can be expressed in *E. coli* strain PEB199. Expression of the GST-Tango-77 fusion protein in PEB199 can be induced with IPTG. The recombinant fusion protein can be purified from crude bacterial lysates of the induced PEB199 strain by

30 affinity chromatography on glutathione beads.

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Example 5: Alternatively spliced forms of IL-1ra and
Tango-77

Computer program Procrustes (Gelfand et al., 1996, *Proc. Natl. Acad. Sci. USA*, 93:9061-9066) is an alignment
5 algorithm that predicts the presence of alternatively
spliced exons for a protein of interest in a stretch of
genomic DNA. Using the IL-1ra sequence, Procrustes was
used to search for the presence of additional sequences
that might encode for alternatively spliced forms of IL-
10 1ra in the two overlapping BAC genomic sequences (see
Fig. 3 and Fig. 4). Potential sequences that encode
variant exons for IL-1ra were identified. These
predicted exons aligned well with the N-terminal region
of IL-1ra, but were not present in Tango-77. The results
15 from Procrustes predicts the existence of more spliced
forms of IL-1ra.

Furthermore, Procrustes also predicted an
additional sequence in BAC1 and BAC2 that encodes an
alternatively spliced exon for Tango-77 (T77-procrustes;
20 Fig. 5). This predicted splice variant form of Tango-77,
T77-procrustes, was aligned with Tango-77 (Fig. 6) and
with IL-1ra and IL-1 β (Fig.7).

PCR primers within this sequence can be used to
generate a product that can be used to screen a panel of
25 cDNA libraries using standard techniques. Suitable cDNA
libraries include libraries made from TNF α -treated
bronchoepithelium, TNF α -treated SSC cell line and anti-
CD3-treated T cells. The resulting cDNA clone(s) can be
isolated from the library and sequenced to identify
30 additional Tango-77 cDNAs.

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Equivalents

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific
5 embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims.

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What is claimed is:

1. An isolated nucleic acid molecule selected from the group consisting of:
 - a) a nucleic acid molecule comprising a
5 nucleotide sequence which is at least 45% identical to the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof;
 - 10 b) a nucleic acid molecule comprising a fragment of at least 300 nucleotides of the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof;
 - 15 c) nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the
20 plasmid deposited with ATCC as Accession Number 98807;
 - d) a nucleic acid molecule which encodes a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID
25 NO:12, SEQ ID NO:13, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or the polypeptide encoded by the cDNA insert of the plasmid
30 deposited with ATCC as Accession Number 98807; and
 - e) a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9,

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SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the nucleic acid molecule hybridizes to a nucleic acid
5 molecule comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10, or the complement thereof under stringent conditions.

2. The isolated nucleic acid molecule of claim 1, which is selected from the group consisting of:

10 a) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10 or the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, or a complement thereof; and

15 b) a nucleic acid molecule which encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the
20 plasmid deposited with ATCC as Accession Number 98807.

3. The nucleic acid molecule of claim 1 further comprising vector nucleic acid sequences.

4. The nucleic acid molecule of claim 1 further comprising nucleic acid sequences encoding a heterologous
25 polypeptide.

5. A host cell containing the nucleic acid molecule of claim 1.

6. The host cell of claim 5 which is a mammalian host cell.

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7. A non-human mammalian host cell containing the nucleic acid molecule of claim 1.

8. An isolated polypeptide selected from the group consisting of:

5 a) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, wherein the fragment comprises at least 15 contiguous amino acids of SEQ ID
10 NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:13.

b) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8,
15 SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid molecule
20 comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, SEQ ID NO:10 or the complement thereof under stringent conditions;

c) a polypeptide which is encoded by a nucleic acid molecule comprising a nucleotide sequence which is
25 at least 55% identical to a nucleic acid comprising the nucleotide sequence of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10.

9. The isolated polypeptide of claim 8 comprising the amino acid sequence of SEQ ID NO:2, SEQ ID
30 NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807.

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10. The polypeptide of claim 8 further comprising heterologous amino acid sequences.

11. An antibody which selectively binds to a polypeptide of claim 8.

5 12. A method for producing a polypeptide selected from the group consisting of:

 a) a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID
10 NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807;

 b) a fragment of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID
15 NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807, wherein the fragment comprises at least 15 contiguous amino acids
20 of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 98807; and

25 c) a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, or an amino acid sequence encoded by the cDNA insert of the
30 plasmid deposited with ATCC as Accession Number 98807, wherein the polypeptide is encoded by a nucleic acid molecule which hybridizes to a nucleic acid sequence of

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SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:6, or SEQ ID NO:10
under stringent conditions;

comprising culturing the host cell of claim 5
under conditions in which the nucleic acid molecule is
5 expressed.

13. A method for detecting the presence of a
polypeptide of claim 8 in a sample, comprising:

- a) contacting the sample with a compound which
selectively binds to a polypeptide of claim 8; and
- 10 b) determining whether the compound binds to the
polypeptide in the sample.

14. The method of claim 13, wherein the compound
which binds to the polypeptide is an antibody.

15. A kit comprising a compound which selectively
15 binds to a polypeptide of claim 8 and instructions for
use.

16. A method for detecting the presence of a
nucleic acid molecule of claim 1 in a sample, comprising
the steps of:

- 20 a) contacting the sample with a nucleic acid
probe or primer which selectively hybridizes to the
nucleic acid molecule; and
-

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18. A kit comprising a compound which selectively hybridizes to a nucleic acid molecule of claim 1 and instructions for use.

19. A method for identifying a compound which
5 binds to a polypeptide of claim 8 comprising the steps of:

- a) contacting a polypeptide, or a cell expressing a polypeptide of claim 8 with a test compound; and
- 10 b) determining whether the polypeptide binds to the test compound.

20. The method of claim 19, wherein the binding of the test compound to the polypeptide is detected by a method selected from the group consisting of:

- 15 a) detection of binding by direct detecting of test compound/polypeptide binding;
- b) detection of binding using a competition binding assay; and
- c) detection of binding using an assay for
20 Tango-77-mediated signal transduction.s

21. A method for modulating the activity of a polypeptide of claim 8 comprising contacting a polypeptide or a cell expressing a polypeptide of claim 8 with a compound which binds to the polypeptide in a
25 sufficient concentration to modulate the activity of the polypeptide.

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22. A method for identifying a compound which modulates the activity of a polypeptide of claim 8, comprising:

- a) contacting a polypeptide of claim 8 with a
5 test compound; and
- b) determining the effect of the test compound on the activity of the polypeptide to thereby identify a compound which modulates the activity of the polypeptide.

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GTCGACCCACGCGTCCGCAGACGTCTACCTGGGGGTCCCGTCTGCGCTCCCGGGATGGAAAACGCCAGGGGAAACTTA 79
GGCAGGCGAGCGGACGGGCACCTCCCGCGGGACGAACTCACTCGGTGGCCTCCTACTTCCCCGGCCGTGTCCAACGCC 158
TGAGAATAACGGGAACAGCGGTCTACTCACCAGACAGCGGCAGCAGCGGCCTCTCTCAATTGGGCAAAGCACTCCAGAC 237
CTTTTGGGAAGAGTGACACCAAAGGCAAGCACCTGCTTGGCAGGCCCTCAGCTTCTACGCAAGTATAAGTCTTGGACTT 316

      M   S   F   V   G   E   N   S   G   V
CATTCCATTTTCTGTTGAGTAATAAACTCAACGTTGAAA ATG TCC TTT GTG GGG GAG AAC TCA GGA GTG 10
      385
K   M   G   S   E   D   W   E   K   D   E   P   Q   C   C   L   E   D   P   A   30
AAA ATG GGC TCT GAG GAC TGG GAA AAA GAT GAA CCC CAG TGC TGC TTA GAA GAC CCG GCT 445
G   S   P   L   E   P   G   P   S   L   P   T   M   N   F   V   H   T   K   I   50
GGA AGC CCC CTG GAA CCA GGC CCA AGC CTC CCC ACC ATG AAT TTT GTT CAC ACA AAG ATC 505
F   F   A   L   A   S   S   L   S   S   A   S   A   E   K   G   S   P   I   L   70
TTC TTT GCA TTA GCC TCA TCC TTG AGC TCA GCC TCT GCG GAG AAA GGA AGT CCG ATT CTC 565
L   S   V   S   K   G   E   F   C   L   Y   C   D   K   D   K   G   Q   S   H   90
CTG GGG GTC TCT AAA GGG GAG TTT TGT CTC TAC TGT GAC AAG GAT AAA GGA CAA AGT CAT 625
P   S   L   Q   L   K   K   E   K   L   M   K   L   A   A   Q   K   E   S   A   110
CCA TCC CTT CAG CTG AAG AAG GAG AAA CTG ATG AAG CTG GCT GCC CAA AAG GAA TCA GCA 685
R   R   P   F   I   F   Y   R   A   Q   V   G   S   W   N   M   L   E   S   A   130
CGC CGG CCC TTC ATC TTT TAT AGG GCT CAG GTG GGC TCC TGG AAC ATG CTG GAG TCG GCG 745
A   H   P   G   W   F   I   C   T   S   C   N   C   N   E   P   V   G   V   T   150
GCT CAC CCC GGA TGG TTC ATC TGC ACC TCC TGC AAT TGT AAT GAG CCT GTT GGG GTG ACA 805
D   K   F   E   N   R   K   H   I   E   F   S   F   Q   P   V   C   K   A   E   170
GAT AAA TTT GAG AAC AGG AAA CAC ATT GAA TTT TCA TTT CAA CCA GTT TGC AAA GCT GAA 865
M   S   P   S   E   V   S   D   *
ATG AGC CCC AGT GAG GTC AGC GAT TAG 179
892
GAAACTGCCCCATTGAACGCCTTCCTCGCTAATTTGAACTAATTGTATAAAAACACCAAACCTGCTCACTAAAAAAA 971
AAAAAAAAGGGCGGCCGC 989

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Fig. 1

1
 IL1ra-human MEICRGLRSH LITLLFLFH SETICRPSGR KSSKMQAFRI WDVNQKTFYL 50
 T77-human ~~~~~~
 IL1b-human ~~~~~~
 Consensus ~~~~~~

 51
 IL1ra-human RNNQLVAGYL QGPNVNLEEK IDVVPIDPH. ALFLGIHGGK MCLSCVKSGD 100
 T77-human ~~~~MNFVHT KIFFALASSL SSASAEEKS. PILLGVSKGE FCLYCDKDKG
 IL1b-human KALHLQGQDM EQQVVFMSF VQGEESNDKI PVALGLKEKN LYLSCVLKDD
 Consensus ~~~~~~

 101
 IL1ra-human ETR..LQLEA VNITDLSNR KQDKR.FAFI RSDSGPTTSF ESAACPGWFL 150
 T77-human QSHPSLQLKK EKLMKLAQK ESARRPFIFY RAQVGSWNML ESAAHPWF
 IL1b-human K..PTLQLES VDPKNYP..K KMEKRFRVFN KIEINNKLFE ESAQFPNWI
 Consensus ~~~~LQL~ ~~~~~~F~F~ ~~~~~~ESA--P-W--

 151
 IL1ra-human CTAMEADQPV SLTNMPDEGV MVTKFYFQED E~~~~~ 192
 T77-human CTSCNCNEPV GVTDKFENRK HI.EFSFPV CKAEMSPSEV SD
 IL1b-human STSQAENMPV FLGGT.KGGQ DITDFTMQFV SS~~~~~
 Consensus -T-----PV ~~~~~~F--Q-- ~~~~~~

FIG. 2

>Contig1

GAAGTGAAGATATAATGTATAGTAGTAATATATAATGTTAGGTGAATTAA
AGGAAATAGAATATATTGGGGAGTAATTATGGGTGTAAAGAAATATAGTA
GGGAAGTATTTAGATTTGAGAAAAAAGGAATTTAGTGTAGGTGAA
NAATAAAAGNANAAGGTTAAAAATTAAAAAAATTAAATATAAATAAAT
AAATAAAAAATAAAATAAAATAAAATTTAAAAAATTAAAAAATATAA
AAAATAAAGAAATGGAAGTGGATTCTTAGAAAAAAGAAAGTAAGGTGA
TATGAGGAGATAGAGAGGATGTGGTGTGAGATGATTGGTTTAATTAGAAA
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AGAGGGTAATGTTGTTTGTAGTGAAAGAAAAAATGGTATATTTTATAAAA
TAATGAGGAAAGTGTGTGAAAAAAATTATTGGGATTGGGAAGGTGAT
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GTTATTTAAAGAATGAAATGAATTTTGTGTGTAATTGGGGATAAGAA
ATTAATGTTTAGAAAGAAAGGAAAAAATTGAAGAAAAAATTAGATTT
TGGAATTTAAAAATATTGTGGGTGTAAATAGGAAGGATTTTAAAGGTA
ATTGTGAAGGATTTGTGTGGAATAATAGGGAGAAAAAATGGGG

>Contig2

GCATCTAACTGGAGCCTGCATTATTACAGATTTAGCATCACCAAAGTCTA
AACAATTAGACTGACTAAGGCAGAACTGCCCTTATGACAGCAGACATAAG
AAGGAAAAGGCCAAAACACTGTGTTAAAAATTATCCAAATGTGAGGAAAA
GGCAAAGAGAGTAGGTGTGCCCTTTTAGTGTCTAAGCTGCCTGCCCAAGG
GGCATCTGATGCTCTCAGGCAGGAGTCCACAAATTTTTTTTGTAAAAGA
TCAGATAGTAAATCTTTTCAGCGTGAAGAGCATGAGGTCTCTGTCCAAA
TACTCAACCACCTTACAACATGAAAGCAGCCAACAGACAACACATGACA
AATGAGTGTGGCTGTGTTCCAGTAAATCTTGATTACAAAAACAGGCAAGA
GGCCAGAGCTGACCCATGGGCCATAGTTTGCTGACCCCTTCTGTAAAGGA
AAGTATTTTGTGTTGACTTGCTGTTTACCATTGATTGAACACAAGGCTCT
GTAAAGTTACTTGTTAACTTGCAGAAGATTGATGAGTGGCAAGTAATTTT
TATTCACCAGAATATAAAATTATTTCTGTTCACTAGAAAAGATAAACCAA
CTGTGATATTATGGTCCTG

>Contig3

GGGGTGTCTGTCTACCATGTGCTCGCAGTTCTGTAATAAATGTTCTCTCA
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AGTTTTTAAATATATATATATATATATATTTTTTTGAGATGGAGTCTT
GCTCTGTGCTCCAGGCTGGAGTGCAGTGGCGCAAACCTGGTTACCCACAA
CCTCTGCCCTCCCGGGTTCAAGCGATTCTTCTGCCCTCAGCCTCCTGAGTAG
CTGGGACTACAGGCGCCCGCCACCACGCCCAGCTAATTTTTGTATTTTTA
GTAGAGACGAGGTTTTACTATGTTGGCTAGGCTGGTCTCAAACCTCCTGAC
CTTGTGATCTGCCCGCCTTGGCCTCCCAAAGTGCTGGGATTACAGGTGTG
AGCCACTGCACCTGGCCAGTTTTTTAAATATATTTTTTAAAAACACTTGAA
TAAGAGTCAGTGTAACCTAGAAGTTTTAAAAATGCTTCACAGAACACCCAG
GGTTTACATTACAAGATTCTCACAACAAACCTATTGTAAAGGTGAGTAAG
GCATGTTATTACAGAGAAAAGTTTGGGAGCAAACTGTAAAAAATTATAT
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TGTTGATTACTTTAAGTGATTTTCCTTGAGAGCACATGATGATCC

>Contig4

GCCGTTTCATAGAAAACCTGAAAGCAATAAGATGACTAGGTAAGCATGACAT
TTAAAGGTATTTCATGGGACGTGGTTACAAAACCAACTCACAACATAAAA
GTCTTAGGACCTCTCGCTGACTTAGGAGCCTGATCCCAACTCTGAGAATG
ACTCAGTGTGTTACCCTGTGGCTAGTGTAGACCAATGATCCTGTCTCAGA
GTCAGTAGCCAAACAGCCCATATCAAGTACTTGAACTTTGACTCAGAAAC
CTCAGTGTGCAACCTTTGACCTAGGAACCACTGTAGTGGTTAACTGCA
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TTACCTTGTAATTCCAATTTGAAATGTGTAATTGACATTAGACTTCTATT
TGAATTTGAAATGTCTAAAACAATGTGGTTAAGTTTGTAAAGGTGTGTG
AATTTTGAGTCTGATTTACTACATTTTTTTTTTAATTTTCTTTTTTTTGG
AGTTTTAGGGATTGCTTAGATGGCTAGAAAGATTTTATTCATCAGATTTT

>Contia5

>Contig6

>Contig7

>Contiq8

>Contig9

4/118

TGTGTGTAGCTCTATGCAATTTTATG1...GTAGCTTCATGTAAACACCC
AATCACAATACTTAATACTATGCCCTCATCACAAGACTCTCTCTTGCTATGC
TTTACAGCTGTATCCTCTTCATCTCCAAACCTAAGCCCACCTCACC GCC
TCCACCATCTCTAATCCCTGGCAACCACTATTCTGTGCTCCATCTCTGTA
ATTAATTGTGTAAATTAATGTTATACAAATGGAATCATGAAGTATGTGTC
CTTTGAGATTGGGCTGTTAATTTTTCTACTCAGCACAATTTCCGTGAGTCT
AATCCAACCTGTGTGTAGCAGTAATTCTTTCTTATTATTGCTGAATAAT
ATGCCATGGTATGGATGTATCACAGTGTGTCTAATCCTTTGCCCATTTGAA
AGGAATTTGGATAATTTCCAGGTTTTGGCTATTATGAATAAAGTGAACAT
AAGACATGTGTGTACAAATTTTGGTGTGATCAAAAGTCTCATTTCTCTGG
GATAAATGCCCGTAATGAAATGGCTGGGTTGTGTGGG

>Contig10

GCAAGAACACAGGCGCTATTATAACCTTACTACCAAGACCTGAACCCAT
ATAAAGGTTTATGCGTAACAATCATCATCCCTGTTCCAGAAGATTACACG
TACGACCACGCTGGCTCACCAGCTCACGTGGGCCAGTACCAGAAATTCT
CCCAAACAAACAGTCGTGTCTGAAAACAATCGCGGTGACCTCCACGGTTA
GAAAAGCCTGTTTTCAAGTCCTGGAATTGCCACATATTAGCTGGGTAAT
TTGGGCATCACATTTACTCTCTCCGAATTTGAGATTGCAAAAACCTCATTG
GATTGTTTTGTGGATTGAAAGAAATAATGTAAATTTAGGCCGAGTGCTTT
GACTTACGCTGTAAATCCTATCACTTTGGGAGGCCAAAGCAGGAGGGTCA
CTTGAGCTCAGGAATTTGAGACCACCTCTGGCAACATAGTGAGATCCTGT
CTCTACAAAAAATTTTTTTTAAATTATCCAGCATGGTGGTACACGCCTGT
ATTCCCAGCTACTCAGGAGACTGAGGTGTGAGGATTGCTAGAACCTGGGA
GATCAAGTCAACAGTGAGCCGTGGTTGTGCCACTGCCCTCCAACCTCAGT
GACAGAGGAAGACCCTGTCTCAAAAAAAAAAAAAAAGTAGTAAGTTTAA
AGAACTTAGTGTAGGCCTGGCATATAAATGATATTGTTGATGTTGATGTT
AGCTTGAAGGCACATTTATAGGAGTAGGGATTTTATAACATTATGAGCCT
GAGAGCACATATAATGTTCCC

>Contig11

GGTCTAACATGCTCCAACCTGAAGAAACCCACACTTGTCCGGCAAGGAAA
CTACTACAGATTTCTGACCTACTGTGCAATTCGGGGCATGCGACGGGAC
TGTGTTTCTGGGTACGCTGTCTCAGGTTCTGTCTGGGATGTAAGAATTCAA
CTTCAGTAGTTCTCTCATAGACGCCGACGAGAGGGGCGTCTCTTTTCTCT
GATGAATCTGCCAGATCTTCCACTTCATAGAGTCTAAATCCTCCGATTCTG
ATCTACTGGAGACCCCCACGTTACAAAAACGTCTAACGTCCGTGACAGCT
CCCCACATAGGGAAAGATCACCTGAGTCTCACTACCTCACATTAGTGCTA
TCTCCAGCCCCATGCTATCTACGAGATGGTCACGCGAGGTTTAAGGGGTC
TCCGATTCCGGTGGTCCGATTACGCTAATCGTGGCCCTACGTGAACGATC
ACTCCTGCTCGTAACATCGATACAGGGTCGCGCTGACAAATGGTACTACG
TAGGTTCTCAGGTCAATGCCGCGTCACGAATGAGCCTAACTACCCATAA
GTGCACGTACTGTGTTACCTTTCTGTTCGGCCAAACCTGCTACTGTATG
CTGTGCTTGTTT

>Contig12

AGGCTCCATGTGCTCTAGCCTGATTATCTTTTCAAGTGTTTTATTTGCTA
ATCTATAAGGCCCTTTTCGTAAATGTTCACTCATTTTCTAATTAGATAT
TTTTTTTAATGTTGAGTTTTGAGAGTTCTTTAGATATTTTAGATACAAGT
CCATTGTCAAATATGTGATTTACAAATATTTTCTCTCAATCTGTAATTTA
GTTTTCATCCTCTTAACAGGGTCTTTTGGAGAGCAAATAATTTGATTTTCA
ATAAGGTTCAAATTATTAATTTTTTCTGTATAGTTCACTTCTAGTGT
TAAGTCTAAAAACTGTGCCTTGTCATAGGTACCAAGGTTTTCTCCAGTT
TTTTTTCTAGAAGTTTAGAGTTTCATGTTTTACATTGGAGTCCATGATCC
ATTGTTAATTAATTTTTGTATATAGGTAGATGTTTAGGTTTAGGGTTTTT
TTAAAAAAAATTACATATGTTTAATTGCTCCAGTTCCCTTTTCATTGAAA
AGGGTATCCTTCCTCCATTGAATTGCCTTTGTGAGAAATTAATTGGACAT
ATTTGTGTGAGTCTATTTCTGGGCTCTTTATCATGTTACTTTTAAAAAAT
GCATCAGTTCTCCACCAATACCTCATGTCTTGATTATTGCAGTTATAT
AGTAAGCCTTAGCATTAGGAAAAGTGTTTTTCTGCTTTATTCTTTNTCA
AAAAATTTTTGGATATTCTAGGGCCTTTACATATAAATTTTAAATAACT
TTGTCTATGTCTAACCAGAAAGCCTTATGAAGATTTTGATAAGAATTGCAT
TATGCCATACATTAATTTAAAAAGAACTGATGTCTTTATTCAAGTTGATT

CTGCTAATCTATGAACA1AGCATCTCT...CAAAGCATTTAGTCTTTCTT.
AATTTCTGTCTAATATTTTAAAATTTTCATCCTAAAGATTCTGTATAT
GTTTTGTTGAATTTATGCTTAAGCATTTCACCTTTCTTGGTAACAATTATA
AATGATTTTGTGTTTTTATTCCACTAGTTCATTTTCAGTGTGTAGAAAA
GCAATGAATTTTGTGTGTTGATCTTTGTTCCCTACATCTTGCAACATTAT
TGAACCTATTATTAGTCTAGGAGGTTTTTTCATTTTCTTGTAGATAC
CTTGAGATTTTCTATATAGACAGTCATGTTGTCTGCAACAGGCACAGTT
TTATTTCTTCTTTTCAATCTATATGCCTTTTTTTTTTTTTTGCCTTAT
TGCAGTGGCTAGAACTTCTAGCACTATGTCAAATAGCATTGGTGAAAGCA
GACATCCTTGTTCTTGTCTTAGAGGAACATTTGGTCTTTAATCTTGGAT
TGCG

>Contig13

GCGCCTCCTTTTCTCTTCCAAAATTTCTCTTGTCTAGTTATTTGTCCAGG
GAAATTTGAAAGCTCACTTACTGTGCAAGTCAGCAGGAAACAACTGGGTC
TGTGCACAGCACCTAGCAAAGTTCTGCTCTAGGAATTACACTTTGGCCCT
GAGGTAGATTTCTACAAGAACCTTACCTTCTAAGCAGCACTGGGGTTTCAT
CTTTTCCCGCTCCTCAGAGCCCATTTTCACTCCTGAGTTCTCCCCACA
AAGGACATTTTCAACGTTGAGTTTATTACTCAACAGAAAATGGAATGAAG
TCCAAGACCTAAGGAGATAGAAAGGGGACCAGTTATGGCATCTTCTCACC
CCAGGACACCTTGCTGCATGTCTCTAGTGCTGAACAGACCACTGGCCTTG
CTCTGTAGTTTGAATGCTCGCTGCAACCAGAAAGGCACCAAGGGGCCAG
ACCATGCTCTCCTGTCTATCACGCCTTCAAAGCAGAATTTCCCAAACCTT
GAGTCACAGTGCTAACACACGGGGTGCCATAACATTTTGTGATTTTGG
CATTTTACAAAATAAAAATAAAAAGTTAAAAATGCATTGCTCTATTCTT
GGGGCTGGCACACTATTGCCTTTGGCCAAATCCGGTCCCTGACTGTTTTT
TTAAATAAAGTTTTATTGAAACACAACCATGCTCTTGTGTACATATTGTC
TCTTGGCTGCTTCCAAGCTACAATA

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GTGTTGCTTTTAACTTACCTAAAATTACTCTGTAATCCATGGATCC
TTAATTTATTTAAAAAACTAATGTTAATGAGTAGCTTTATTTTCTCCCA
TCTAATTTAAGGCCACAGAACACCTTCACTTACCTCAATCCTCTCCCAA
CTTACATGCTTTTAAATGTCATATATGTTAATACCGTATACTTTTAAACT
TTCTAAAATAGCATTATTTTATAGCATGAGTGTTCAATTACATTTTGTCA
TATATTTAGAATTTTCTTTGCTCTTCGTTTCTTCTTCTATTATGACTCC
CCTCTGGGATCATTTTCTTCTACTTGAAGTACATAGTTTAGAACTGCAC
TATTCAATACAGTAGCCACTAGCCATGTGTAGCTATTGAAGTTTAAACTA
AGTAAAATTGAGTAATATTA AAAA ACTCAGTTCCTTCTACTAGCCAC
ATTTCAAGTGCTCAGCAGCCACGTGCGACTAATGACTACTGTACATCAA
CATATAGAACATTTCCATCATGGCAAAGAGCTCTATTGATAGTGTTTCATC
CAGAGTTTCTGTTCCAGGACCAAACCTGAGGGTTGGGCTGCTATTTCTCAT
GGCCCAATAACAAGATGCAGATGAGCTGGGGAGGAAGAGAGTTTTTATTT
CTGCNACCATTTACCGGGAGAAGGCCTGGAAATCATCACCAGGCCAACTC
AAAATTATTACGTTTTCCAGAGCTTATATACCTTCTAAGCTATATGTCTA
CGTGTAAGTGTGCATTACCTGAAGACGTTAGTGATTAACCTCTTTTAAAT
CTGTAACCTAAGGTCTGAGTCCGGAAGATCTTCCCCTGGAGCCTCAGTAAA
TTTACTTAATCTAAATGGGTCCAGGTGCTGGGGTAATTACCCTTATCTTG
TCCCCTGCTAAATCATGGAGGTTTGGGGATTCTTTAGAGCACCAATAAAA
CTTGTTTGTGGAGGCCTGGGGGTTTCTTCTGACCCACAATAAACTTGTT
TAATCCTAAATGGGTCTGTGTTAAGAATCCTTCTTTATTTTGTATATTT
TAAGGCCAGAAAAGGCCTGGGCAAACTCTTGATGGGCTTTTGTACAT
TCCAGCCTTTGTATAAGAACACTGGTTTTTAAATATTAACTTAACCATTT
AGTCAGTACTGAAACAGTTGTTATAGAGATCTGCATTAGTGAGACCTGGC
CTGCCACATTTCTTTTCTGAAGATCTTATGGTAGTGATCACCTTTGTGA
AAGGAAAATAAATCTTGGGACCTCAAAATCACTAAGCCAAAGAAAAAGT
CAAGCTGGGAAGAATCTGACACTTAAATCCAACACTGCTAACTCATTCTAT
CTCACTCATTCACTTTTATTTTCTTTTCTTTCTTTTCTTTTCTTTTCTTT
TTTTTTGAAACGAAGTCTTGCTCTGTCAACCAAGCTGGAGTGCAGTGGAT
CTCAGGTCACTGCAACCTCCACCTCCCGGGTTCAAGCGATTCTCCTACCT
CAGACTCCTGAGTAGCTGGAATTACAGGCACCTGCCACCACGCCTGGCTA
ATTTTATATTTTATAGTAGAGACGGGGTTTACCATGTTTCATCAGGCTGG

TCTCGAACTCCTGACCTCGTGATCCGC...CCCCCTCGGCCTTGTGTTGCT
GAGGTACTGTCTAAATGCTGGAAGTGAAGTGGCAAGCAAGACATCCCTA
CCCTTGAGGAACTGTAATCTAGTCGGAATACAGATGTCAACCAAGTCT
CACACAAGAAATTGTACAAAACCCCTAGGA

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GGAAAAACCTATCACCGCTCCTATGGAAGTTAAAAACAAAAAGAAAGTA
ACAAAGGAAATGAATATTTTCAATCTGGAAGAACATTGAAAAAGAACAGGA
AGAAAGAGAAAGCACAACTCGAACTGTCCACTAGAATTGACAACACTCTGA
CAGAATGTCTGAACCTCATCGAAGGGGTAAGTGAAAAAATAAGCTCCTC
CAGCTTTGGCCCCAAAGTCTTATAATTTTTTAAACATATTCCTAAATATAAT
ATAGGAGAGATAGCCTTCATCTAAGTAGAAATTTAGCTACTCTTGTAAT
ACAGAGTAATAATAATGACATGCCCATAAACAGTGTCTTTGTGTAT
CTGTGCTTTTATAAGCACTTAGCTAAGATTATCTCACATAATTATCATAA
CCACTGTTACTATGACCCTTTTACAAACAAACTGAGGCACAAAGAAAGTT
GGAAACTAATCCAAACAACTGGCTCCAAAGGAACTTTGCTTTCTTTG
GGTATCAAGTTCTGAAGAGTACACATTTAACATTGAACTGAGGTCAGAA
GGCAAGTTTCTATGTAAAGTTGGAGTATTCTGAATACTCTGGGTAGCTAC
AAATAGTATTTAAATTTTATCTTGGATTCTGCAGATAAGGATAAAATAGA
TGGTAGGCAAAGAGTATGATCCTTAGGAGAAATTTTTCTGAAGGAAAAA
TATATTAATAAAAAATGATGGAATAAACTTCTAAGATCCTTGCTAGAGC
AAAACCTCATTGAGTCCTTTGGCTGGTAATGTTGAACATCAACAAAAAAA
GGAAAAGTTCAGTTTAAAGTCTACTCCAGGCAACATTTTCAACATCCAG
TTAAATATTAACATTTTCTCTTTGTGGAATTGAACTAGAGTTCTTTTCT
TATCCTCTTTTTTGGTTGTGTATTATTTAAAAATGAGTACCTTTTATT
ATTGAAATCATTTCAGTAATGCAGATAAATGATCAGCCCTCTCCCTGTA
CAACATACATACTTAGGCATCCCAAACCTCTCTCTGGAGGTGACCACCA
TTGCCAGTCATTCTGTTTTCATGCATGTCCATACAGTATAGGTATG
TCGAGAAATGAAGTATTATTTTTGTGAGTTGCAATTCTTTTATTCACA
TTTTTGTGTACTTTGGTTGTCTTTTCTTGTTTCTTAGTACCAATGTT
ATGCTGACTTAGGCAGATGAGTTGAGTATTTTCTTTTGGCCCTATAAAC
TGAAAATAGTTTGTATGACATGAGAATTATTTTATTTTGAAGGTTG
ATAAAAACCTTGCCCATAAAAATCGTCTGGACCGGTTTCTTGAGGATGCCT
GTGTTAGAGCC

>Contig16

CGCTTTAACCTGGGCTACCAATGGTTCGTCAAGTTCTAGATTCTCTATTA
ATACCTTTTTCTTGTTCTTTCTCTGGTCTGTTTTAGCCCCGAGTCTCT
TAGATCTGCTCTAATATTCCTATTGACTTTACTTCATTTTCTAAGTCT
TTATCCTTTTGCTTTTACTTTCCGAGAGACCTGCTTAACCTTATCTCCAA
CTCTTTTATTGAATTTTCAATTTCTTTTACTATATATTTTACTTTGAATA
CACCTCTCTCTTCTCACATTTTCCCCCATAGTATTTTGTCTTCAATTGA
CAGTTCTACTATCTTATTACTCTGGAGATATTAATAATAGTTTTTAAAT
TTTATTTATTTTATTTTCAAAACAGTGTCTTACTCTGTCACTCAGCTG
GAGTGCAGTGGTGTGATCATGGATCACTGCAGCCTTGATCTCTGAGCTCA
AGCTATCCTCCTGCTTCAGCCTCCCAAGTAGCTGGAACCACAGGCATGTG
TCACCATACCCAGCTAATTTTTTGTGTTTGGAGGTGGAGTCTCACTCTGT
AGCCCGGTCTGGAGTGCAGTGGTGCATCTGGGCTCACAGCAACCTCTGC
CTCCTGGGTCTGGTTCAAGCAATTCTCTGCTCAGCCTCCTGAGTAGC
TGGGATTACAGAAACACACTACCATGCCCAGCTAATTTTGTATTTTGT
AGAGACAGGGTTTACCATGTTGGCCAGGCTGGTCTTGAACCTCTGACCT
TGTGATCTGCCCACCTTGGCCTCCCAAAGTCTGGGATTACAGGCGTGAG
CCACTGCACCCGGCCACTAATTTTTTAAATTGTTAATAAAGACGAGGTCTT
GCTATGTTGCCCAGTATGGTCTTGAACCTCTGGGCTTAAGTAATCCTCCT
GCCTCAGCCTCCCAAAGTGTGTTGGGATTACAGGTGTGAGCCACTGAATCTG
ACATTTTTTAAAGTTTTCTTCTCTTTACCAAGTCTTTTTTCCCCTTTCT
GCTTTTTTGGGTTGTTTTATTTTGTATCTCTATCTTGCTAGAACTTTCTG
CAGACGTTTAGTAATACTAGATTTTGGAGAGTGGGCAACTGGAAAGCTGA
TTGGAAACTCTGAATACATGGGTGAGGCTTGTGAGTGTGAGTGTGATG
CTTGATGTCTGCAAGGCCAATGGGTTTGGGACCCCTACTATTAGTATA
GGCCTGATTCCCTGGGAAAGGCTCTTTTGTATCTCTGCTGGAGGATAAA
GGCCTGGCTACCAGCCTTCTGTGTGTAATGTGAGGGAGAAGGGCTGGAGT

FIG. 3 (5 of 52)

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ATTCAACATCATGCTGAA.CCTTTCAA.LATCATCTTGTTTTTAGTAATC
TCCTACCTTAACTCTCTGTCTTCTGCTAGTATGGGAAAGATGACCTGAAA
ATCTAACCATTTATTTTTCCCCATTAATATCATTTTATGATTATTCAGA
AGTTAAATAATTGTCTGCTGTCTCTCCAAAAAGACTGAATCAACTAGCAA
CAAATAAGAATTTTCTCACAGCTCTGCCAGCATTTTAAAAGAATAGCTTT
ATTGAGCCCAGGAGGTCAAGGCTGCAGTGAGCTGTGATTACACCACTCTA
CCCGAGCCTGGGTGACAGAGCAAAACCCTGTCTCAAAAAAGAAATTTAAG
GAACAGCTTTATTGTTGTAAAATAGACATACAATAAACAGAGCACATATT
TAAATTGTGCAACTTATACTTTGATATAACCCTGTGAAAACATCACCACA
ATCAAGATAGTGAATATATTTATCACCTCCTGATACAGTTTAGCTCTGTG
TCCCCACCTAAGTCTCATGTTGAATTGTAATCCCCAATGCTGGGGGAGGG
GCTTTGTGGGAGGTGATTGAATTGTGGGGGTGCACTTCCCCCTTGCTGTT
CTTGAGATAGTGAATGAGCTCTCATGAGCTCCCCCTTCACTCACTCTCTTT
CCTGCTGCCATGTGAGGATGTGCTTGCCTCTTCTTTGCCCTTCTGCCATG
ATGTGTTTCTGAGTCCTCCCTAACCATGCCTCCTGTACAGCTTGCAGAA
CTGTGAGTCAGTTAAATCTCTTTCTTCATAAATTACCCAGTCTCAGGTG
GCTCTTTATAGCAGTGTGAAAAGGAACATAATACCTCCTAAGTTACCTC
AAGCTTGTTTTTTAATTCCTTCTCCTCCCTTCTTCATTGCCAAGCAAACA
ACCACCTGTTTTCTGTCACTATAGATTAGTTTACATTTTGTGGGTTTTTT
TTTTTTTTGAGACAAGGTCTGACTCTGTTGCACAGGAGCAGAGCAGCGTA
TC

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CGCGTTATAGGAGATGCGAACTTAAGAAATGATGATAAGGAGACTTTATT
AAATATAATTTTGAATTATTTTGCCATTACAGAAATTCTAATTATTTAAA
ATTCTATTCTAATTTTTAATCACTGTACTTCCAAGCTTAGCTTAGAAT
CCTTCTGTGCTGAGGATTAATTTAATTTGTCTTTTATAGGCCTTATCTA
AAATCCAAGAATAATTGCCAGAATCAACCACCTTCTAAATCTGTAAGTAG
AAATTAGTCTTTTTTAAAAATATGCATTTCATAAGTATGATTAGTAATAAAA
ATAATAAGATGTTAGCAACCTAAAGAACATGTATTTGAAAGGTATTTCT
TACAGATATAAAAACAGTTTGGTTTAATAAGAGACAATCATTTTTTGA
AGTATGACATTTTTTGAAGTAGTTTAGTTTTATTAACCAAGAAAAGCC
TCAAGTGAACTTTAGTCCTCTTGATAGCTAACATTTATTGAATGCTTACT
GTGTGCCTGATACTTTTCTGACTTGCATTACCTCACTGAGTCCTCACAAT
CTTATGAGGCTACTATTAGTAGCCCCACTTTACAGATGAGCAAACCTAAGT
CACAGAAAGGTTAAATAGGTCGTATAGCTATTAAGTGACAAAGCTGAGAG
CCTGTGATCTTAACCACTTTGGTATGCTGCCATGAAGTTAAATAGCTCAG
TAGTCATTAAAGAGAACATTTGCATTGAACCTTCCAAGCCACTTAACAA
GTATGCTTCTCTAATCAATTTAATTTAGCTACATTAGATAGAATGGTAA
AGGATCTCTTAACTTAAAGTTTAAATGGAAGAAATTAGCCCTCTGAAAGAG
GCACAGATTATTCATCTGCAATAAAAAATCTCACCTTTAGTTTTTTAAAC
ATAGTTTTTATCTGTGTTCTGAAATGTAATAAAACAGTGCTTCTGAAG
TGAAAAATTCTCACTGGTGAGAATTTAATAAGTTTTAATGATTCACCAA
ATCACTTCAGTCATATTTAGTCATATGCATATGCATATATAGACATATA
AGTTTTTATCTGTGTTCTGAAATGTAATAAATAGTGCTTCTGAAGTG
AAAAATTCTCACTGGTGAGAATTTAATAAGTTTTAATGATTCACCAAAT
CACTTCAGTCATATTTAGTCATATGCATATGCATATGTAGACATATATA
TGTTGTATGTATACATGACATCATTAGACACTGTGAAGGATAGCAAAATG
TATATAAGGCAAAATTTATGAACAATGGTTTAAACGTTTGGGAAGCACTGG
GTTACACTTTTACTTTATGCAGATTGAACCAGTATAGTATGCAAGTCTTA
AGGAAAAATCTACTGGAAAGGGCCCTCATTACAGACTTCCCAGAGGCTTCT
CTGGAAGTTGACAATACTGACTTCAGTACATCAGCTCGTAAATGAGGATG
ATACCTACCTTATCTGCTTTACACAGTTGTAAGTAAAGTGAAGTCA
GGAAGGGAATTACAGAATTTAGGAGAACTAAAAGCAGATGTAAATAAT
AGTCATCATTACAGTTATATAATGCTTGACAATTTATATAACACTTTCTGA
TACATGACAACAATAACTAACACCCAGACATGTTTATATACATTACCTCA
CTCAGAACAACCATGTGAGGAAGTTGGCCATATGCTTTAATGTCCAAACC
AGGACACTTTTGAGAGTAAAAGCAGTACTCTTTGACCAACAGGCATATAA
TCAAACTATCTTGTGAAAACCGGATATATGGCATCCTTCTAGATAAT
AGTACTTTTACTATTATTAATTTGCTGTGAATCTAAACCTGCTCTAAA
AAAGTTAATTTTAAAAAGTAATGAAGTACTGATACATGCTACAACATGGG

FIG. 3 (6 of 52)

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TAAATCTTGAAAACGTTATGCTAAGTG...AGAAGCCAGACAGAAAAGGCG
ACATATTACATGATTCCATTTATATGACACATCTAAAATAGGCACATCTA
TAGACATACAGAGACAGAAAGTAGACTAGCGGTTGCCAAGAACTGCAGGG
AGCAGAAGATGGGGAGTGA CTGCCAATANGAAAACGCATTACGT

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TGAATCGCAATGATATGTGCCACTTTGCACTCTCTGTGACATATATAATT
ATTTTTAATGCATTCAATTTTTCTCAGAGTGCATTTCGTTTGAAAACATA
GACGGGAAATACTGGTAGTCTTCCTTGTGAGTTAGAAACACCCAAACAAT
GAAAAATGAAAAAGTTGCACAAATAGTCTCTAAAAACAATGAACTATTG
CCTGAGGAATTGAAGTTTAAAAAGAAGCACATAAGCAACAACAAGGATAA
TCCTAGAAAACAGTTCTGCTGACTGGGTGATTTCACTTCTCTTTGCTTC
CTCATCTGGATTGGCATATTCCCTAATATCCCCCTCCAGAACTATTTTCCCT
GTTTGTACTAACTGTGTATATCATCTGTGTTGTACATAGACATTAATC
TGCACCTTGTGATCATGGTTTTAGAAATCATCAAGCCTAGGTCAGCACCTT
TTAGCTTCTTGAGCAATGTGAAATACAACCTTTATGAGGATCATCAAATAC
GAATTCATCCTGAATGACGCCCTCAATCAAAGTATAATTCGAGCCAATGA
TCAGTACCTCAGCGCTGCTGCATTACATAATCTGGATGAAGCAGGTACAT
TAAAATGGCACCAGACATTTCTGTCTCATCTCCCTCCTTTTCACTTTACTTA
TTTATTTATTTCAATCTTTCTGCTTGCAAAAAACATACCTCTTCAGAGTT
CTGGGTTGCACAATTCTTCCAGAATAGCTTGAAACACAGCACCCCCATAA
AAATCCCAAGCCAGGGCAGAAGGTTCAACTAAATCTGGAAGTTCCACAAG
AGAGAAGTTTCTTATCTTTGAGAGTAAAGGGTTGTGCACAAAGCTAGCTG
ATGTACTACCTCTTTGGTTCTTTTCAAGACATCTTACCCTCAATTTTAAAA
CTGAGGAACTGTGACATATTAAATGATTTACTCAGATTTACCCAGAA
GCCAATGAAGAACAATCACTCTCCTTTAAAAAGTCTGTTGATCAAACCTCA
CAAGTAACACCAAAACCAGGAAGATCTTTATTATCTCTGATAACATATTTG
TGAGGCAAAACCTCCAATAAGCTACAAATATGGCTTAAAGGATGAAGTTT
AGTGTCCAAAAACCTTTTATCACACACATCAATTTTTCATGGCGGACATGT
TTTAGTTTCAACAGTATACATATTTTCAAAGGTCCAGAGAGGCAATTTTG
CAATAAAACAAGCAAGACTTTTTCTGATTGGATGCACTTCAGCTAACATGC
TTTCAACTCTACATTTACAAATTATTTTGTGTTCTATTTTCTACTTAAT
ATTATTTCTGCAATTTTCCCAATATTGACATCGTGTATGTATTTGCCATT
TTTAATATCACTAGACAATTCAATCAGGTTGCTACGTTGGTCCCTTGGGT
TACTCTAAATAGCTTGATTGCAAATATCTTTGTATATATTATTGTTTTT
TCTCCTATCTTGTAATTTCTTTGAGCACATCCCAAAGAGGAATGCCTAGA
TCAATGGGCACAAATAATTTGACAGCTCTTATTAAACATTATTCTGTAAG
TAAAAACTGAACCTACTTTTCAGTATCACTAGCAACATATGAGTGTATCAG
CTTCCTAAACCCCTCCATGTTAGGTCAATTATGAACCTATGATCTAACAAA
TTACAGGGTCTTATCCCACTAATGAAATTATAAGAGATTCAACACTTATT
CAGCCCCGAAGGATTCAATCAACGTAGAAAATTCTAAGAACATTAACCAA
GTATTTACCTGCCTAGTGAGTGTGGAAGACATTGTGAAGGACACAAAGAT
GTATAGAATTCCATTCTGACTTCCAGGTATTTACACCATAGGTGGGGAC
CTAACTAC
CATGCACACACAATCTACATCAACACTTGATTTTATACAAATACAATGAA
TTTACTTTCTTTTGGTTCTTCTCTTCCACAGTGAAATTTGACATGGGTG
CTTATAAGTCATCAAAGGATGATGCTAAAATTACCGTGATTCTAAGAATC
TCAAAAACCTCAATTGTTTGTGACTGCGCAAGAAGAAAACCACCCATGCTG
CTGAAAGTCAGTTGTCTTTGTCTCCAACCTTTACTTCTTTTACCTCTCAT
ATGTTTGTGAATAAGCCCAATAAGCAGACNCCTCCTACAAAGTGAACCTG
GTCTCTTCTCCTAACAGGG

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GTCTTGTAACACAGGTAAGACGAGTTCAAGTTTTATTTCTTGNTTTTAGA
ACGGTAGTGAGCGGTTTTTCAAGNTGAGACCACACCTAAGGTAAGTAGCTG
AATTGGGGTTTTTGTCTTGGCTAAAGTTTAAACAACCAGCTGGTCTTAATTT
CTCCTTACCATTAGAGCACTCAGTAATCATATAAGTTGTGTGATCATTCA
TTTTGCTTAACTGTTTGTCTTCTGTTTTATTGCTGTTTCAGTCTTTTTCC
CATGGGTTTGACCTACTCTATCTGACTTGATCAAATCCAAAGGAAATTT
CCAAATTATGGGGAATGAGGCCTCTGAAGTGGCTAAATTTCCACCCCTCCC
ACACACACAAACGTGGTATGGTGGGGGAAAAAACGCCAGCAAAAAGAAAA
AAAAAAGGAAAAGATGTTTCATTTTGACCACCAACGGGCTTTATTAC

ATAACAAGGCCACCTTT...GCTAGCCA...CCATACTGAAAGAGCAATGL...
TGTTGCCCCATGCTGTGGGTTCCATAGCTAACGTTCTGCCTTTTTTCCCTA
CCACGACAGCCTGGGTTTGGTTCCCTAAATCAAGCCTTTTCTGGTTTGATA
CTTGGTAATGCTGAAATAGCAGCAATTGTCTAGCTGAAATATCGTAAT
AAGATTTTAAAAGATTTATTTTAAAGGACCTCAATAGTTAAAAGTCAGCT
TAATTTAAAAGCTAACATCCAAGATGTGTGCATGTGTATGTATGCGTCTTT
GTATTTAAATAGCCCTCATGTTTTTTTTTTCTTCTAGGAACCTGCCTT
TTTTTGAGCAAAAGTTTTTTTTCTTCTCTGTTGACTGGATTCTGTTTTCTT
CATTACTTCTGCTGTCTCTCTCTTCTCTTGCACCGTCTGCTGCATGAGA
GCCCTAAAATAGTTTATAATAGCCTGGGGTTCCTTAAAGAAAATGGAGAA
GGTGCCAGGCTCCCTTTTAGGGAGAACTTCTATTTTCTTATGGAATC
CCTAGAGTGTAACAGACAAGTTCATTTAGCTCTTAAACTGCTTGCGTT
TGTGTTGTGTTACCTGATTTTTTTGACTATTATATTTTACTAGCTATT
GCAACAGAAGCTACTCTTGGGTTTCAAGGAAGATTGTAGTTTAGACATG
TAGAAATGTCTTTTAAAAAACAACCTTTTTTTTAAAGTGCAGTGTAA
AAGCATCATATGGTCTAGCCTCCTAATAATTTTCCCTTTTGGAGACCAG
GATTCAGGGTGGGCTCTGCCCAGAGCTCAGAGATCCAGTTAAAAGAGAGG
TAGTCTCGGCCGGGCTAGAGGCCAGCCTGTAATCCAGCACTTTGGGA
GGCCGAGGCGGGCGGATCACGAGGTCAGGAGATCGAGACCATCCTGGCCA
ACATGGTGAAACCCCGTCTCTACTAAAATACAAAAATTAGCTGGGTGTG
GTGGCAGGTGCCTGTAGTCCAGCCACTCGGGAGACTGAGGAAAGAGGAG
AATCGTTTGAACCCGGGAGGCGGAGCTTGAGTGAGACGAGATGGCGCCA
CTGCACTCCAGCCTGGCGACAGTGAGACTCCGTCTCAAAAAAAAAAAGAT
AGGTAGACTCGATGTTGTCTGTAACCGAGCAAGTTAGAGCAACGCCCACT
TTGAGACGAATTTAAGAGTCTTTTATCAGCCGGCGACCAAGAGACGGCTA
ACGCTCGAAATCTCTCGGCCCTTGGGAAGGGGCTTGATTTTCTTTATG
CTTTGGTTTAGGAAGGGGAGGGGAGCTCAGTTGCAACAATTCTACAGGAG
TAAAAACATGCAAAGAAATTAAAAAGACAAGTGGTTACAGGGAAACAAAC
AGTTCAGGTGCAGGGGCTCTAAATCTATCATAAGATGTTAGGTATGGGG
GCTCTGCCGGACACAACTCAAGGCTTTATGCTGTTATCTCTGAGCGAA
ATCCTGGGAACCTCGTACATTGCTTGCTTCAGTACCTTATCAGTTAATCG
GACTCTTTGATATGTTGGGAGTCAGCGTACACAAGTTAACTCCTTGAGGA
AGGGGGTGGGTAAGGAGTCTTTGATGTCTGGTAAATGAAGGAGCGAAATC
GAGTTCCTCTGGCTTTCTCAGCTAAGGGAGAGCTTATTCATGTGGAAACA
AGGCTAAGTGATTAAGGGAGAAAGGGAGAGTCTGAAAACAAGGTAGGTA
TTACAATGTCATAAAATTGGTCTCCTTATACAGTCTTATGGTAGATTTT
TTTCCATCTTTAATCTCCTCTAGCACCACCAGACTTTTTCTCTCTGTAC
CTTGAGATGTAAATTTTGCTATCTGAATTTTCTGCTAAGAGTTGTTTCT
TTAATATGCAAATTTAGGGTTATTTAGCTGACAACCTGCCAAAGTAGTGAA
ACAAGTTATCAAGAACTTGAACGTCTAAGGTAGGAAAAAAAAAAGTCTTT
ATGAATCTATAAGATGTACTTCTATTGGCATGCCTAATACGTCTATGTAT
TTACGTGTTGTGTACACAGTTTTTCACTACTGAAAATATATAGAGGAGTT
CTAATTAATTGACTTAAGACAATAAAAGCGCTTGAATCAAATACCTTATC
AGGAAAAAGGAAAAGACAAGTCAAATGCTTGTTCAGTCTATATACTTA
AGTAAATCTTTAATAAATAAGCTAGCTTTAACATTATTTGAAATGTCTT
AAGAATTGCCAGCAGGTTCTGGGTTACAGAACTAGTGGGGGTGCAGTGGG
GTGAGGGTTGGTGGGGTGGGNGGTNNNACNNNNNCNNCCCCCCCCCCCCC
CCCCCCCCCCCCCTCCCCCCCCGCCCCGNGCGGCGCGCCCCCCCCCGC
CCCCCGGCCCCGCCCCCGCGCCCCCACCCCCCCCCCCCCCCCCCGC
GCCCCGCCCCCCCCCGCGCCCCCACCCCCCGCCCCCCCCCCCCCGC
CCCCCCCCCCCCCACCCCCACACCCGGCCCCACACGACCCCCCACCCGAC
GCCCCGCCCCCCCCCCCCCGCAGCCGACGCCCCCCCCCGCCCCGCCCCG
CCCCGACCCCCGACCCCCCCCCGCGCCCCCGCCCCGCCCCCCCCCGC
GCCCCCCCCCGCGGCGCGGCGCCCCACCCCCCCCCCCCCAGCCCCGACC
GCGCGCCCCCCCCACCCCCCCCCCAGCCCCCGCCCCCGCCCCGACCC
>Contig20
GGCAGTACGCTATAATTCCCTCTTCACCTTACCTCATCTGTTCTCTGATG
GATGTACTTTTTTTTTTAGTTTCTAAATCCCTTTTCTTTGCTCTGGAG
ATGGGTGATTGATGTAGTCTGGGTATTTGTTCCCTCCAAATCTCATGTTG
AAATGTAATCCCCAGTGTGGAGGTAGGGCTGGTGGGAGGTGTTTGAT

FIG. 3 (8 of 52)

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CATGGGGGCAGATCCC. ATGAATAGC .GGTACTGTCCTCTCAATAG. 4
AATGAGTTCTCCTGAGATATGGTTGTTTAAAAGTGTGTGGCACTCCCCCA
TTGCTCTCTTGTACTGCTTTTCGACATGTGACATCCCTGCTCCCCTTCGC
TCTCTGCCATGATTGAAAGTTTCCTAAGGCTTCGCCAAAAGCTGAGCAGA
TGTGGGTGCCATGCTTGTACAGCCTGCAGAACTGTGAGCCAAAATAAACT
TCATTTCCATATAAATTACCCAGCCTCAGATATTTCTTTATAGCAACATA
AGAGTGGCTTAATACAGGCTGGGCATGGTGGCTCACGCCTGTAATCCCAG
CACTGTGGGAGGCTGAGGGGGGTGGAACATGAGGTGAGGAGATTGAGACC
ACCGGCTAACACGGTGAAACTCCATCTCTACTAAAAATACAAAAAATTAG
TCGGGCGTGGTGGTGGGCGCCTGTAGTCCCAGCTACTCTGGAGGCTGAGG
CAGGAGAATGGCATGAACCCGGGAAGCGGAGCTTGCAGTGAGCCGAGATT
GCACCATGCACTCCAGCCTGGGCGACAAGAGTGAAACTCCATTTAAAAA
GAAAAACAAAATTTCAAACAGAACAAAATGAAAAAATACCAAGTGAAA
GGCCCTATAAAAAACCCCTCTGGGGCCCATCTCCACCCCTCAAGTGA
AACCACATTTAACAATTTGGTGCATATCTTTCCAAACCTTTTGTGTACA
CATATAAAAAACATACATGCTTTGATTTGGCTCAGACTGTACATAGTGTT
TTCCCTCTTGCAATTTTACACTTAATATATCTTTGACATCTTTCTATGTCA
GTGCATGTTGGCTCGATGATATTCTATCATTAAATACCCCTTCAAAAATG
GTAAATCATTTTAAAAAATCATTACACAAGTACATATTTACAATTTTA
AAAGAAAACAGAATCCCAAAACACAACGACAAACCTCTAAAAATAATCTC
TATCTTTCCACCAGCATGGAACAGTTTCATTCTTTTTTACATAAAACGAA
TTATGTGATTGGAAAGATTAACCTCTAATCTACACATTTATATACAGAATG
TTCTATTTGTTAAGCCTATCTGAAAATAAAAAATTGAGATGATTAATTCA
CTTACACTTAGAAATTAAGTCAATATACTATGAATACACATTGTGATCAG
TTATAATATGATGCTTCTTAGTCTAGGGTTTCAATTAATAACAGTAAAA
AAAATTGGATAAATAAGACAGCTAATAACTGAAAAATCCAGAAATTCAAA
GATTATATTGCCAACTAAAACACTGCCATTTACATTTTTTTTTCTACTT
GGTAGCAAATGCTAATGGAATTCAATCCTGATTACTTAAAGTCAGTTCAC
ATCACACATTCATCAGGATAATACGAACATAATATGCCTACTATAGCGT
TAGATTAAGACATAAAATTTTTTTGCTTGAAAGTAATGACTGCGTACCAC
TTGAGACATTTGTCAACCACTTCAGCACATTGTTTACGAGTGACTGGATG
TCCACAAGGAATAAAAACGACAGCAATATTTCTATCCATACAGATTTTGC
AAAGCTTCTCCTCTTGAGGTGTCTTAGCTGCTCTTCAGTACTAATCTCT
TTCTGCAATGAAGTCTGACTTGATTTCGTCTTGTGTACTGTCTTTCTGAGC
CTTCACTGGATCTGCAATCAGAACCTCAAGTGATTTACAGTTGCTCCCAG
ATGTCTGAATTTTTTCTCCATTATTTTCTTAATGTCTTTGAAACTGAAC
CCCATTATATAGCTTCTTGTACCATAGGATTATGGAAGATGGTATCAAT
TTTTCTAGTTAGTGATGGCGTTTTTTTTCAGCAGTTCTTACCAGACACTCCT
CAAGTGAATGGGATAAATGAATATTGTTTATATATTTTCGTGTCTTCTGT
TCTAACAGATATTTACACCCTGGATGCCATTAACATGTTGTCCCAAGGGT
CTTNTCTGGGCT

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CTTTCTCCCTTTTTACCCCCATTTTCGTAGGGATTGGTTAAAACCCATG
TAAAAAATCCAAACACCGGCGGGGAACGGGGTTCAAGCTCGTATCCCCA
CCACTTTGGGAACCCCAAGGTGGCAGGATTGTCGGAAGCCAGGCATTTGAG
CCCACCCTTGGGAAAAAAAAGAGAACCCCATTTTTTTTTTGAACAAAAC
CCAACCCTCCAGGAAAGAAATAAGTATGGCTGGGTTGAAGTCACCAAAG
ATGGCCGACTGGCTGGTCAAGTAACTTTACCTGATGGTTTCGTAGAATATT
TACCTTCACCCAGGTGGGAGAATTGCTTGAGCCAACCCTCAGTGTGGATT
CAGGAACCTTGATTTAATTGGTATCGTGATTGTGGATTAGATTCTCAGGGA
TGCATTCACTAAGTAAAAGTGATAATAGCTACTTTTAAGTAAAATAATGA
ATGAATCAAACACTCTAAATCCATGGTGCTATGCTAAGCTCTTTCTGTAT
TTTATCTCATTGATATTACAAATATTTGATGTGTTAATAGTAATGACTA
TCTCCATTTTTACAAGTAAGGAACTGACATTGAGAGATTAAAAGACTAG
CACAAATCACAAAGTAAATGAGATTGAAATCCGGTCTTGATTCCAAACTC
TACAGTATTCTAAATTCAGGAGACTAAATTATAAGATGGAGAGCCAATT
TTACTTTATAACAGGGTTAGAATGGCAGAAGAGACCTGACATTCACACCT
CTAGCCAGTGATCATCTTCTGTAGGCAAATATGCAGGAAATCTATAAT
AAGAACGTCTTTTGGTGAAGGCCAGGTGCAGGGGCTTACACTTGTAATTC
CAGCACTTTGGGAGGTCAAGGTGGGAGGGTCGCTTGATGACAGGAGTTTG

FIG. 3 (9 of 52)

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AGAACAGCCTGGGCAACATAGTGAGACCTGTCTCTACAAACAAAAACA
ACACAAAACAACTTCAAGAAAACCTCTTTGGTATGGATCAGAACAGATG
AATTATCTATCTGATCCAAATGCTTAATGACATTAAGCCACAGTCCACTC
ACTGCCACAATAGAGATATACCTGCCAATGCCACTCAGGTAATCCCATCA
AAAGTGGTAATGAGGTCTGCAGCATGACTTGTTCTTAGTGATCCAGCCT
GAGACCTTGAGATTGCAGCATTTTATTCTACATATGCACAAAACATCTGT
TGAAAAATCTTCTAAATTGATGCAATACATTTCGTATCAAGAATACCTGTC
TGTAATCTCCATAAACCCCTCTCCTTTCTGTTTTAAAAAATAGTAACAGCA
TTTCTCCTTACATGACAAAGAAATGACTTCACCATCTACGAAATAGTGAA
TAGGAGCTGTGTGGAAGGAAATTAGCTCTACTTCTTGGTGGAGATGAGAA
GGGAGTGTTCTCTGAAAATCAAGGCTCTTGTCATGCTAGGAGCCAAAGT
CGTTTTTTTAGAGTGTGGACAGTTGAGAAGATAAGACAGGGACCATCCACT
CATGTTTTTCTTATTCCATAGGCCTCTCTCAATTGGGCAAAGCACTCCAG
ACCTTTTGGAAGAGTGACACCAAAGGCAAGCACCTGCTTGGCAGGCCCT
CAGCTTCTACGCAAGTATAAGTGAGTATATAAAATGGGGTACTTGTGCT
GTTGAGTACCTTATTTCCAAATGAGGCCTGCCGGTGTCCCTGTGGCTGTG
AGAAGGCCTTACTGGATAGGTGGAAGTTGTGTGTTCTCATCTTTCTAA
CCCTGGATTGACTTGCCCAAAGGAAGCCATTATTAACACTATAATAAAA
CCATCCTTAATCTGGGACTCTCTTCATGCAGTGGTTCTTAACCAGTGATA
AACATGAGAGTTACTTTTGGAGCTTAAAAAATTAAGATGCTCAAGGTCT
ACCCAACTGACTGAATCTCCAGAGGTGAGGCCAGGGATGTATACTTTT
GAGCCAGACCTCAGTTTACCCTGCAGAGCTCATAAGGTTGCATAACACCC
TTTGTCAGCCACTCTGATGAAAAGAAAAATTGGTGAGGAATAAGTTTTAG
AGAAGAAGGAGCAAAGGTGTTCTTGGCCAGTGAGAGCCAATGACAGGGAA
ATGCAACAATGTATCCACAAGAAAGGTAAATTACCCTATAGAGCATTTT
AGGATAAATGAACATCTCATGCCTAGGGTTGAGAGAGGGTACAAAAAAA
AAAAAAAAGACCCTCTGGATACACAACGCGATAAATGGAATAAAGAA
TTTTTTCCTTGTAATTAAAAAATCCTTTGTACTGAGGTATAATTTAA
TCTATTTTATGTATAGTTCAATGAGGTGTTATAGATAATAAATTTTTTT
GTAAATTATTATATTGTATATACTCATACATTCATTTTTTAAAGTCAGA
AATGTATATAACCATTAACTTATAAATCATTCAAGTCATTTCAGAGATATA
GATACAGGAGCATATTTTATATCCACCACAATAATTATTACCATCTCAAC
AATTCCATCACCCCTCAAATTTCAAGCGTAGGGTTTTTTAAATGTCAAAG
GAGTCTACTCAGTGGGAAGAAAGTTAAGGAAAAACCTTTGGGGCTTTGG
GCTCCTTCCCCCTGGGGTTAAAAAGGCAGGAAATTGGGCTTACCCCCCT
GAAATTGGGAAGTCAAATTTTGGGAAGTTTAAAAA

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TCAAGCAGCCTTCTTCTTGGCTTCCCAAATTGTTGGGATTACAGGCAT
GAGTCAGGATTCCTGGCTTAGTTTACATTTTCTAGAGTTTTGTATAAATG
GAAACATACAGAAATGTATTTTTTTGCGGAGTGGGGGAGTGTCTTCTATTTC
TTTCTTTCCATTTTCCCCCCCCNCCCCCGAGACGGAGTCTCGCTCTG
TCTGTTGCCAGGCTGGAGTGCAGTGGTGGATCTCGGCTCACCGCAAGC
TCCACCTCCCGGTTCAAGCAATTCTCCTGCCTCAGCCTCCTGAGTAGCT
GGGATTACAGGCGCCCGCCACCACACCTGGCTAATTTTTTTGTATTTTT
GGTAGAGACGGGTTTTCAACATGTTAGCCAGGATGGTCTCGATCTCCTGA
CCTCGTGATCTGCCGCTTCGGCCTCCCTAAGTGCTGGGATTACAGGCGT
GAGCCACCGTGCCCGGCCAAGTGTTTCTATTCTTAACCAGCTTTCATG
CAATCTTTTTTTTATTTTTACCATCTCTGTGATCCCACTCCCAAAGGTACTA
GATGTCGATTGGTCTTAGGATCAGCTACCATTGCCCCAAGTCTTTCCA
GCCTTCCAAAAATTTTTTTCTTTTTTTCTTAAAGATACTCCTGTGTGAGG
CTCAGAACTCTTGAATTGCTACTGCAAATATGAACTCGGTGATGTGAATG
CCAGGGAATTGCCTGATTGATCAAAGAAATGTATCCCTTCTCCCTCACT
CTTGCTGTCTTCTCATTTGTTTTCCCATCCTTGTGGATTCTGAATTTA
AATATCCCTTTAATGTTATAATATTTTAAATGGCGTTTGGCGAAAAGTACA
GAATTAGGTGCAAGAGTGATAGCTGTTATTTTTTTTTTGGCCTCTGAGA
CTGTTTATATATGCAAGTTATTTAACAGAAAGTTCTGCAGTGACCTGAGA
TGTCAGGGGGGTCTGATAGAGTACGTTTGAAGGCAGTTACTGGAAAAAA
TAATGCCATTCTGGTTTGTACTTCGGTAAGTTTCAAGTACCCAATATAT
TGTTTTACATGTGGCATTCAAGTAAAAAAGTAGCTTCCCTCCTTTCTTCT
TCCTTTTCTCCTTCTCTGCTTCTATAAAGCATCTGCTTTGGGAACTTCT

FIG. 3 (10 of 52)

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TAGGAGGAGAGCTTGCCAGCCCGTGGC AATGGAGAGGTCTTGCAAGAGA.
AAAAGAGATGCTCCCACTCAATGCAGGATGGTGTGGAGGTAAATGGGGAT
ACGTCTGGCATCACTCAGGAATGGGCCTTCCTGGCAGGGAAAAAAGGGA
GGGGAAGAGGAAGGGAATTCNNANATNAATTGCTGAATACGGGGATTCC
ATGGCCTGGATCCAGGAAGAGAACTTTGGGAGGTGTGAACCTGGAAGGCA
TCANCTGATGAGGAGCAGCCTGAACTCCGGGGAGGACCTGTTTTTGGTGG
CCCGGAAAAAATGCCTTCCACACACAGGGAGGCCACCCGGCTGATGGGC
TGGGGGTGGACGGACAGCCCTAGGACAGGCTTGGGAAACCAGGCTCAGG
TAGGGCCTGCGAGGTTCTCGCTGCGTCTCTTTCTTCTTCTGCTTTAGAAA
ATAGAATCCAAGGCCTCTTGAGAGTGGAAGGTGGGTGGGAGGAGGGCAG
ATGGGGCTTAGGCCCAGGACACCCGTAGAGCTACTGCCAGCTGTCTCTC
AGGGACTCTGCTGAGGTCACTCCAAGGATCATTCTTAGCCTTGCTAGACA
GTACTGACAGAGGGAACCGTAGTATCGCACCCACTTCCTTCTCTTTCAAT
GAAAGTTTAAAGGTCACCATTTCCTCTGGCAAAGGAAGTTCACAAATAT
TCCATTTCCGGTCTTAGAAACAGCAAGGTATCAAGCAATTGCAAACTTCC
TGTGCTGGGGAATTCCTAAGGAAGTAGGGGCAGAGTTCTGGTGGAGACAA
AGTGAATTCGAGTGATTAGTCAGTAGCAGTAGCAGTAGCAGTAGCAGTA
GCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGCAGCAGAAC
AGAATTTCCCGCACGTGTCTCAGGCTCTCATTGCGCAACTCAGTCTCTA
AGTATTTTTATTGGCAGGAAAAATAAAATAGCTATGAGTGAAATAATTCA
TTAGACCTGAGCCTCCATCAATTTTGTGTTTAAAGGCCTGACTCTCTTTA
CCTTTCCCTGGGATGGAAGATGCAAAATGTTCTGATCTCACTGTCAAAAA
AGAAGAACCAGTGGGTATATTGTATGCTTGAGTTCCAGCCATTAGTCACA
AGACATAGAGATGACTGCCATGTGTGTAGACTTTCTATAGACTGTGTGCT
AAACCCGACCTGCCACTTCCAAGGAGTAGATGAGGAATGTCCATGGTTCT
GGGGAGCCCTACCCCAATTTGGGGCAGACATTCCAAAGCTCATTCTTCTGT
GGAGGGGGTTGATGGTTAAAGGAACGGCTGGGATTTACTCTTCTTTCTAG
GGCCAAGAAAATGACATGCTGCCTCCATGTTTAAATCATCCTTCCCCCTGT
TAATAACTATGGCTTTAAGTCCCCGGTTAGGGCCTTCCTCCAAAATTGGG
GAAAAAAATTCCCCTCCCCCCTAAAAATTTTTTTTTTAAAAAACCTTT
TTTTTTGGGGGTTGGGAAAAAACCAAAATTTTTTTTCCCAGGGGTTT
TTTAATTTAAATTTCTCCCCAAAAATTTGTTTTTTTTTCCGCGAAAAA
AAGACCCCCCAAAAAAAGGTTTTTTGGCGGAAAAAATATTTTT
TTTGTGTTAAGAAATGGAGAAGAAGGGGGTTTTTTTTTCTTCTCCCC
CACCSCCAAAGGAAAGGTTGTTACAGATTGTTTTGTGTCTCCCGCCCA
T

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ATGTGCCTGCGAAATCATCCTTCCAGAAATATTTGCCCTTTCTTTTGT
ATAGAGTGGCACTGCCCTATATGGTGACCACTTGCCACATGTGGCTGTTG
AACACTTGAATTTGGCTTGTGAGAATTGCAGTGTAAGTGTAACACAT
ACCAAATTTCAAGACATGGCACATAATAAAAAATGTAAATATCTCATT
AACATTTTTATATTGACTGTGTAAGTAACATTTTGAATATATTGGATTA
AATACATGGATGATGCCCCAACCCACAGTCCCTTATCAAGTCTCTACT
TCACATTTTTGTACTTCTGACTTAGAAATAGCACTGGCGTCTAAGAGCCT
ATTAATGTGCTCAATAGGTTCTTGGGAACCAATTTTAAACAAAATGAC
ATATAAGAAAAAGCAATAACATTGAACAAAATGACATTATTGAGGACCTG
CTGCAATGTTGTTTCACTTAAAGTCAAGTGTCCAAGAACTATCAGTGACAT
TTAGTGAGGAATTGCTGTCTTCTGTTTACAGGAACCTGGGCAAGTTAC
TTAATTCCTCTAAGCCCGGTTTATATCCCTGCAAAGAGAGAAGGATAATA
ATCACCAGTACTTAGTGATGTCGTAAGGAGAAAAATAAATAATAATATG
AAATGGCTGACAGTGTCTTGTGACACAGAAGATGTGTGATCCACAGTAG
CTGCTATTGTCTGCCTCACTTCACTAGTAATGGTCCAGGGAGGCCTTTAA
TGTGCATGGTGACATTCACATGTTGGACATGGGTGAAGGGAAAGAC
CAGGCTCATCTAAACACAATAGGATGCTTGTGGTGTGTTTGGAGGGAATC
AAGGACTAGTTATCCACAGCTGTAACATGCATGGATCAAAAGAGATAAGG
CACACAAAAGACTTTGTGAGTAGCAAAGCATTACAAAATGCAGAGACCAG
CTGTGGGTGGTGGTGAGTCAGACCCAGCTTCCCTCTGTGCCTGGCTGAGT
GGTTCTGGGCAAGTCACGCCATCTGTCTTGATGCCCTTCCCCATCTATAG
AGAGGGAGCAACTGAGGCCCTTCCAATACTGAAGTCCTTTATTTCTGCT
ACTTTAGAAATATCCACATTTTTGGTAAATCAAATGATCCAATGATTCC

FIG. 3 (11 of 52)

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ATTCCTAATGTTCAAAACAGCCCCAC AACATCTAAATGAATCAAAAC
AATAAAATATTTATTGTGTATGTTTTGATTGCTGAAACTTCTATTTTAGC
AACACACACACACACACACAGAAGCCATAAGCCTTCATCTTTCCTTGGAT
AAACGAGCCTTCCTGTCTGGCCATTTAAGTCACGATTAAGTAAATGATT

AATAAACTAAGATAAAC AGAATAATTAAACTTAATTTAAAAGAACA
 GGAAAGGAAGCAGTTACATTAAGCAAAAGAGACATCTTCATGGTTGAAGA
 AGTGTATGCCCTGGTGTCTGGATCCCATTAGGAACTGGTAACCTTGC
 AATCTTGGGCAGATTGCTTAATTTCTCTAGACCATGACTTCCTCTTCTGT
 AAGATGTGATAAGAACATCTACCTCACAGGTTTCATGAGAGGATTAAATG
 AGATAATGTATTATAATCCCTTGAACATGGTAGGCTGTTATGTTAAGTCC
 TTTCTCTCTTCTCTGTAGCTATCATGGAATTTAAAAACACATTATAACTA
 GAGCATGAGTTGCGACTAAAGGCTCAATTGTCTCTGCATGTGTTGGCTCA
 TGCATGCTTTATTCTCTGAAGAGCTTTTATACCAAGTGAAAGGAAATAA
 TTGCATTTCCCTGAAAATTACAGGAAAAAGTTATGTTTTTCTCTTCATT
 CAAGTGATTCTGTTAGACCCAACCACATGCAACAATTTTAAAGTTGCTTC
 CAAATATATTTACAAATATTTCTGTCTTCAAGGAACAATGGCAAGACCA
 TGACTCAGGTTTACATCCGGATTCCACCACTAACCATGTACCCAATTACT
 TCAGTCACCTTTCATTGAGTCTTACATATCACAGAATAAAATCAGATTTT
 ATCAGAGGAGGTGAAGACAGGGAGAGATATTTCAATCCCTTCTCCGC
 AACCCCGTTTTTTTTTTTTTTTTTAACAAGGATCCTAGAGTTACTGAATG
 ATAGCACGTTTGGGGGAAAGACCTAAGGATGATCTTTATAAGCCATC
 ACTTGGTGTGGTGGTGATAAAAACTCGAGTATCTTTATGCAGTGGAAA
 GAGAAGATTGGACTCGGAATCAGAAGCTTGAGTTCAAGCACTGGTTTCAT
 CAGTCTTGTGATCTTGGGTTGGTCACTTAACCTCTTCAAGGGTCTCAGC
 TGTGAAAGAAGATAGTATCAGCTAATTCCTTGTATGTGCAGTGAGGAGGCA
 GTGAGATAGTGCAGGTAACTATAAAACAATTGTACATGAAACGCATCA
 CAGTGATTCTTTGGACCCACAAGCTCCAATCTTATAAACATATCCAGTC
 ACCCACCACATAGATCATCTCACCTTGCATATCTGATTTTGTGGATCAT
 GGGGAAAACTGCTGATTCCCTAGCAAAACCCATGGCATAGGATAAGTGCA
 CAATAATTTTTTTTCTTAAATGATTTAGATGACAGTGACTCATTAAAGG
 TTTCTGAGGCCTCCTCAGAGTCGAGAGGTGGGTGCCTGAAGCCACCCAA
 AGTCCCTGTACAGGATGGCTCCCAACGCACACACCACAGGCCTGCCCAG
 TATGTTCCACTATCTACCCAGTAGAGCCCTGCCAGTACGTTCCACTGTC
 CCTTCCCTAGAAGAGGTGACTGTTGTTACAGTCCAGAAAAGCGGGCTC
 CCCAAAACAATGCAAGGACCCACCTCTCTCTGAACCTCACCCACCTAGT
 TTTCTTTAAAAATCAATTTACAAGAAGATCATGTGAAGGAAAAGGTTGG
 GTGATATTCTAACCCAAGTTAGCTGTTTCTCAACCAAGTTCTCTTTGAAA
 AATTCAACAACCACCTTTGGGGAATTATTTACAACAGAGGAGTGAGGATG
 GGACAGGATAGGTATTGCCTATGTTGGTGGAACAGGGTTTTTTCTCTG
 GATTACCAAAGAGATGGTATGCATTGCTCCCAGAAGCTAAATATCTTCAG
 GCTTTCAATGGTGGCCTTCACTGAAAATGTTATCCCTGTTGAAGCTTTC
 AAGCCAGTATTTTCATAAGAACTATATTTTCTTTGGTGAAGTGAAGCATT
 ATAATGATGACTATACAGGTTCTTGAGTGAAGCCATCATTAGCATT
 GTCATTATTTTGTGTTAGTTGCATCTCCATAGCAGCTCACATTCACAATG
 TGCTTTGCAATTGTTCTTAGCAATAGCCCTCACAAGATTCTCAGGAGGA
 GAGGGTTAATCCGGATTAACATTTCTGTGAAGCCTAGCGAGATTAATCGC

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AAGAGTTTTTAAATTAAGTAAGGACGCCGGGAAACAAATCAATCCCAGCA
 AACATTTTGTGGGATTTATCATTCAAGCAATTTTACAGTTATCCCTGTC
 AAATACATTAAGTGTTCAAAATTGGGCATAGGGGGAACAAAATAATAAAC
 CCAGCCAAAACAGAATAATCCCTGTTTGTTCATGTTGGATAAAAAAGAC
 ATTACTATTGGTGTAAAGGAAATTAGATACATCTTCATTATTTAGTAAAA
 TTACCATAACTTCTAACTTTGTGGCTTTAGGCAGTCTAGTCCACAGGCAG
 GAAGGAGGTTTGTGTTGGCAAATGACTGTTATCATCTTCTGTTTCAAAGC
 TAAACCATAAACTAAGTTCCTCCCAAAGTTAATTCAGCATATGCCAGGA
 ATGAACAAGGACAGCCTGGACGTTAGAAGCAAAATGGAGTCAGGTAGGTC
 AGATCTTCTTCACTGTCTCAGTGATGGCAGTTTCATAACTTTAAATGATG
 GCTATCACAGTTTTTATAAATAATCTAGATAAACAGTTAAATAAAATAA
 TTAGGTAAATGTAGTGGATAAATAATTAGTAGACAAACTCACCATAATTT
 AGAATCTAAAGTTAAATTAATAATAATTTTATTATTGTTGTTTCC
 AAGAAAAACATATTGTAGGAAACCATTTCTTTTTAAAAAAAAGTGTCTT
 TTTAAAAAGGTGAATAATTTTGTCTAATTCAAAGTTTATTGAAAAGTTA
 TGTATAAACAAAGGTAAAAGGAACAAGGAAATAAGGGAAATGTAAAGAAA

FIG. 3 (13 of 52)

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ATTATAGAAATAAAGTGCTATTTTTTGGTAAGAAAGCTTAAAGGAGAA...
ATTTTAGGTAAGAAAGAATCTTACCTAAAATTTTGTGCTAGAATAAAGTG
ACTGGCTAAGAAAGGGATGTTCAAAGCTATTTATGACAAACCCACAGCCA
ATATCATACTGAATGGGCAAAAGCTGGAACATTCCCTTTGAGAAGCTGGC
ACAAGACAAGGATGTCTCTCTCACCCTCTATTCAACATAGTATCGGA
AGTTCTGGCCAGGGCAATCAAGCAAGAGAAAGAAATAAAGGGTATTCAA
TAGGAAGAGAGGAAGTCAAATTTTCTCCGTTTGCAGATGCATGATTGCAT
ATTTAGAAAACCCCATCATTTTCAAGCTTAAAGCTGATAAGC
AACTTCAGCAAAGTCTCAGGATACAAAATCAATGTGCAAAAATCACAGGC
ATTCCTATACACCAATAATAGACTAACAGAGAGCCAAATCATGAGTGAAC
TCCCATTCACAATTGCTACAAAGAGAATAAAATACCTGGGAATACAACCT
ACAATGGACATGAAAGACCTTTTTCAGGGTGAAGTCAAAACCACTGCTCAA
GGAAATAAGAGAGGAAACAAGCAAATGGAAAAACATTCCATGCTTATGGA
TAGGAAGAATCAATATCGTGAAAATGGCCATACTGCCCAAGTAATTTATA
GATTCAATGTCTATCCCATCAAGCTACCATTGACTTTCTTACAGAATTA
GAAAAAACTAATAGCCAAGACAATCTTAAGCAAAAAGAACAAAGCTGGAG
GCATTGTGCTACCTGACTTCAAACCTATACTACAAGGCTGCAGTAACCAA
ACAGCATGGTACTGGTACCAAAACAGATATATAGACCAAAAGAACAGAAC
AGAGGCCTCAGATATAACACCACACATCTACAACCATCTGATCTTTGACA
AACCTAACAAAATAAGCAATGGGGAAAATAATTCCCTATTTAATAAATG
ATGTTGGGAAAAGTGGTTAGCCATATGCTGAAAAGTGAAGTGGACCCCT
TCCTTACAACCTTATACAAAATCAACTCAAGATGGATTAAAGATTTAAAC
ATGGCTGGGCATGGTGGCTCACGCTGTAAATCCCAGCACTTTGGGAGGCC
GAGATGGGTGGATCATGAGGTGAGGATGGAGACCATCTGACTAACAC
AGTGAAACCCTGTCTCTACTAAAAAATACAAAAAATTAGCTGGGCATGGT
GGTGGGCGCCTGTAGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATGG
TGTGAAACCAGGAGGTGGAGCTTGCAGGGAGTGGAGATCACGCCACTGCA
CTCCAGCCTGGGCAACAGAGTAAGACTCCATCTCAAAAAAAAAAAAAAAAA
AAAAAAAAAGAGGATTTAAACATAAGACCTAAAACCATAAAACCATAGAA
GAAAACCTAGGCAATACCATTGAGGACATAGGCATGAGCAAAGACTTCAT
GATTAGAACACCAAAAGCAATTGCAACAAAAGCCAATTGACAAATGGGAT
CTAATTAAACTGAAGAGCTTCTGCACAGCAAAAGAACTATTGTCAGAGT
GAACAGGCAACCTACAGAATAGGAGAAAATTTTTCAATCTATCCATCTG
ACAAAGGGCTAATATCCAGAATCTACAAGGAATTTAAACAAATTTGCAAG
AAAAAAAAACCCATCAAAAGTGGGCAAAAGATATGAACAGACACATCTC
AGAAGAAGACATTTATGTGGCCAACAAACATGAAAAAAGCTCATCATCA
CTGGTCTATTAGAGAAATGCAAAATGAAACCACAATGAGATACCATCTCAT
GCCAGTTAGAATGGCGATTATTAAGAGTCAAGGAAACAAACAGATGCTGGA
GAGGATGTGGAGAAATAGGAATGCTTTTACACTGTTGGTGGGAGTGTGAG
TTAGTTCAACCATTTGTGGAAGACAGTGTGGCAATTCCTCAAGGATCTGGA
ACCAGAAATACCATTTGACCCAGCAATCCCATTACTGGGTATATACCTAA
AGGATTAGAAATCATTCTATTGTAAAGACACATGCACATGTATGTTTATT
GCAGCACTATTACAATAGCAAAGACTTGGGAACAACCCTAATGCCCACC
AATGATAGACTGTGTAAAAAATGTGGACGTATACCCCATGGAATACTAT
GCAGCCATAAAAAAGAATGAGTTCATTCTTTTGCACGGAACTGGATGAAG
CTGGAAGCCATCATTCTCAGCAAACCTAACACAGGAACAGAAAACCAAACA
ACAGGGAGGGGAATGTACACACCAGGGCCTGTCAGGAGGTGGGGGGCAA
GGGGAGGGGATAACATTAGGAAAAATACCTAATATAGATGACGGGTAAATG
GGTGCAGCAAACCCCATGGCACATGTACACCTACGTAATAAACCTCCAT
GTTCTTACATGTATCCAGAACGTAAAGTAAATTTAAAAAAGAAAGAA
AGAAAGAAAAGGATGTTACAGCAAACAGAAAGTCCAAGCATGTATGA
ATAGTCTGTGTAAGTCAATAAGAGGATTATTTAAAAAACTTTTATA
TGATAAAGTTGTCTATAATTAAAGGGAAATTATAATGGTCTTTCTAGAGA
TTGGGTTGATGTTAAAAAACTACTTATATATTAATAAATTTGGTTAGAACA
ATGAAATTTTCTTACGGGGTTGATTCACTCTTAATAAATTATAAGAGACT
TAAGAATTTTTTTTAAACCAAAGTTCAGCTTTTATTGCATCTTGCTGTT
TTAGCTTTCTCTCCCTTTTAAAGGGTGGGAAATAGTAATGCCCTCCTT
CAACTCCCTTCAGCTCATATACGTTTTTTACCTCAGATTCTGTTTGTG
TGTCCTGATGCTAACAATGTTTTCTTAAAGGTCTAAAGGAAATGTTTTCT

FIG. 3 (14 of 52)

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TCCAACATAATATTCTGTCATTGCAGAAGGTCTTTTCTTTTGCTTTT
GTAAGTGGCTTAACAGATTTTATGTTTTATTGAAATAATTTCTATGCCAT
TATTATTAAGTTTTGGTTTGCTTAGAAAACACTGAGATTAATACAATTTT
TAAAAATTATGATTATTACATCCATATATCTTTATGTATGTGCTTTTAA
AGTCCTTGTGACATTGAGTTCTAGGGCTTGACTCCTGGGTCTTAAAGGA
CAAGTCTGTCTAAATCTTAAATACTGACAGCAATTAAAGGCTCATCTTCA
GGACTGGTAGAAAATGCCAATCAAATAAACTGCATTCTTGAAACACAGA
GCCAGAAATTAAAGCTATTCAACTCAAGGCCAGGAACATAGTGGAAGA
GGTGGGTGTGTGAGATTGTAAGGGCCAATTTTGAGAGATAAAATAAGTTC
AATTTCTCTATAAATTAATCATAATCATTGATGTCCAAGCCACACTGATG
CAAGATCAGCATATGGGTCTGTGTGATTAACAAGGTTTTCTTGAAGC
ATTAACCTACTCCTTAATAAAGGTTATAGAGGTTATAAAAGGCTTCTGGA
AGTTATAGCTATGGTCAAGATAAAAATTTATAGATTGTTAATACAATTT
TGGAACAATTTAATTGGCTTCTTGCTGTTTTTATTAGGGCTTATTGT
TTGGAACAATTAAGTCTCGTCTCTCAAAGAATGAAGGCTTTCACCTTTTTT
TTTTTTTTTTTAAATCCTTGAGTTATCACTTTGGTCAAATGAATGACTTA
TTTTCAATGACCTTTTCACTCAAGTGTTTTAAACCTTTCAAATTTGACAAA
CTTTCCAAAATCAAACACTACAAATTAATGTCTTTTTTATGACCTAATGAATCC
TTTAAATACTAGGTTCCCTAAAGTCCAAAAAATAAACATAA
TGTGGCTTATTTGGTATAAAAATTTTACAAGAAACATTGTCAAATATAAA
ATATTGTGTGGTTTTGTTGGGCTGTATTTGTATAAATATGTTATTGGTA
TGTGTTCCAAAATTATAGGAACTCCTATAATTCTGATATGACTTGGTGT
ACATTATCAGTAATAATTATAATTGTTATGGTAAATTATTGTGTGCCATG
GAGGTAACAAATTTCTCATCAAGTGTCTTTGACTATGGTTGCCCTAA
AACTTTTGGCATTACAGACAATTGTCTTGCTTTGGTCTCTTTAGAAG
GTGGTTTTATAATCAGCTATAAACTCTAACGGGTGCTCTTGAATGCAGG
CTTAAGATAGCTTTGGAGACTGTGACATCAGAATAGAGGAAAACTTTCA
GTATTCATGGAGTGTGAAATATTATGAATATCAAGCAAAACAGGAATT
AACTTCATAGATGGAACATAAAGAATGCTGAAGTAATCTTTTTGACTTTT
TTTCTTAGAATGTTGATCCTTCGTTTTGTTTTTCAGAGTCNAGGAAATTT
TTCTGTTGAGATATTGACAGCTTTAACAATTAAGTATACTCCAGTGAACA
CAATTGGAGCA

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ATCTAGTCATTCCCCAGCCTGACCAATTCAATGGCCCCCATCTTAGTTAA
AATTCCTCACCTGACAAGGCCCCATCTACGCCTCTGACCTCATGCCCTC
CACTCTCAGTCTTGCACTCACCTGCCACACTCAAGGGCTTCCCCAGGTT
CCTTCTTAGATTCCACCGATAGCTCAGGGACTTTGCACATGCTACGGTCT
CTGCCCTGGCTCCTCCCCAGATCTTCTCATGCCTAGCTGCTTCTCATCAGC
ACCTTCTCAGAGACTGTCCCTGCCCTCCTCCAGGTTCCATACCTGCCA
CCCTCCCCCAATCACGTAACAGTTTCTTCAAGAGCGAGTTACCATCCCA
GTATTTCCCTAACTTATTTTTTGTGACTGGTCTGTTGCCTGTCTCCACCA
CAAGAACATAAGCTGCATGTGAACAGGAGCCTTGCTATCTTGTCAACCC
AGTGGCTGTGACATAACCTGATACACATTAGATGCTCAATGATGTTTGAT
GAATGAAGTGTGGTAGTCCAACCTGTGTTTCTTGTCTGTGTAAGTATGT
CTGTTGTGGTTTCTAAGAACCTACAGCTCTCCCACTGTGACTCCTGTTT
TATGGTCTCTGATTTGCTGGACTAGAATCCTAACCTACATGCTTACTCTTA
GTGTCCTCCCCCAGAGGCTGAATCCAGTCCCTAAACCTCCACCAATGG
CTAAGACTGAGCTTCCAACCAGACAGGCCTACGCTGAGACCTCAGCACCG
CCCTTCTCGGCTCTCATCCTTAACGCATCCTTCAAGGCCCAGCTTAAATG
TCTCTTCTCCAAGGAAGGCTATCCTCTTTCTGCCCTCAGTGCTCTCCAT
GCCTCCTCTATGCCTCCATGCCTGCTTTCAACCTGCAGAAGTGGAGAAA
TTGCTAATCTGCTGTGTTGACACTGTGCTGGGGTGCCTTGGGCCAGGGAG
CAGGCTGGTGGTGTGCTGATAGCCCGTGGCTGTGCCAGGTCCATGCTCA
CTTCTGAGCCCCAGTGGAGTAGGCTCCCTTTCCCTTATTGCAGCACTCA
GAGGAAGGACGTGCTTCTTAGGACAGATCTGGCCAACCTCTCCCTCGTGA
GAGAAGGCCAGCCATCCTCTTGCCCTCTTTCTTCTCCTGCCCCCGAGT
AATAAAGGTGCCTGGTCAAGAGCCTTCTAGAAGGAGACCCAAACATCCACC
ACACATTCCCAGTTCCAACCGTCATCCACATGGCTGGCTGTGCAGGTAAA
CGCAGAGTCTGTTTCAACACCCCAACCATCTAGTATTGGATGGGAGGACA
GTAGCGTGACACTCTTCTCCAGCCTTGAGCCCTACTGTGGGCCCCACCCA

ACCCAGATACCAGAGGAGCCCTGTAAGTGGGATGCTATTGGATGCTTGG
AGTCATGTACAAAGTTAGCCCTTTGTTATATAGAGTTAGCTACGTACATC
TTCCCTCTGTAGGGAACCCAAAGAGGGGAGAAGAGATATGTAGTAGGATTTA
ACCTGCAAAATCCTCTGCTGAGCACCCCTGCACTACATACAGTGGGTAGCAT
GTGGTAGGTGCTCAATAACTATTGACCGATAGATTGAATACAGGTAGGAT
GGTGACACAATCTAAGATCCCAGGGGTGGGGAGACCACACGCTTGGTTAG
GGAGACCCAAAGTGGACCGTGTGGCCAGAAGAGTCCCGCACTGCACTCTA
GTGACAGTGCAGAAAGTCACTGTGGGAAATCTAGAAGTTTCTACAGGTTG
CTATTTTCATCATAGCACTGTGCAGGCCAACCCCTTCTGCTCCACTGGCTG
TTGGGAAAAGCTTTCTCTTTTCTTCTCCTAGCCAGGGAGCTCTCAAAGTGTT
CCACTCTCTCACCTCCACCCAGGCGTCCAGGTGTGGAGGACACTTGCCGG
CTGCTTGTCTGCTGACTCATCCCTTGGTTTCACTTGGAAAACCTACCACC
AGCTGGCCTCTTTCCAAGCATCAGCCTCCTCATTTTCTTAATCCCTTAGG
TGTGATCTCACCTCCACACAGTAGATTGCCTCAAGGCCCAATTCCAATAT
GAATAAAAATGATTATTTTGTCTCTTCCAATCTTCTTTTAAATATTA
TTTTATAATTCCCTTTAGGAGGATCACCTAAGTGAAGACTATTTTACCT
AAGAAATGTTAAATGTAAAGACATGGTTGTAATCTGGGGATTCTCTGTTA
AAATGGCTAGCAGACAGAAGTCAGACGACAGGCTAGAAATGTGTGAAGAG
TGGTTGCCTTTGAAAGGCGGAGTTGGTAATGATTTTCTTCCATTTTCCA
TGCTTTCCAATTCTCTACAAAGGCCTTAATATTACTTCGATAACCAGGAC
CTCTGATAACCTGCCCCACCGAGTAAAGACTTAGCTGGGAAAGTCAGCT
TCATGTGAGGTAAAAGGAACCAGGTAATACACAATTCCCACTGCCAACTG
TCGGGTGTGCAGGCCTGAGCTTCTGTCATGTGGGAGGAAAGAGAAAGAAG
AGAGAAACTCCAAGATCCAAGAGATCCAGCAAGAAGGCTGGAGTCTGAGG
ACGCAGAAAGCTGAATGGCACAGTTACCACTATTGTGCTGAGGTTCTGTG
GCCTCTGGGTCTCTTGACAACTGGGCAAAGACCCACAGAAAATCTCTCT
AGACCTTACCTGTGGGAGGGGAAAGTGCTTAAGATCATTTACAGGACAGC
CACCTGGACCTCAAATGGCTTACAGTTCTTTCATCCAGAGGGTCTTCATT
TAGTACATAACCAGGTGCTAAGCTGGGTGCTGGAGACATGACGGGGAACCC
ATTTACCATGGCTTTGTTACTGTGACATTCACATCTAGGGAAAGCCAGCA
AAGGGGAGGGATCGAGGAGAGCTTGTAGGCAGAGAAAATACCCAAGGGC
AAGGGAGAAGCCAGCCTGTTCTGAGCACACACAGTGGTTCCATCTAACTG
GGCCTCAGTGCCAGGTTGGACTGGAGATGGGGCTGAGGAGCTGTCACAGA
GCATTCTGGACACAGATGTCACATAGTCCCTTGAGGTTAGGGTCTTAGG
CATGGCAGCATTGCTTTGAGTTTTTCTTTTGTAAATGTTGCCATTTCATGA
CAATGTGGAAGATGGGTCTTGCAGAGAAGGGCAGGGCTGTGAGACCAGT
TAGGAGCACTAAGATGTGAGCCAAGGAAAATGAGGAACACCTGAACACTGG
GGCAGGTGCAGGGCCAGAGAGAAGCAGATGGCTTCTGAGGTTTTTAAGT
AGGTAGAATCAAGGCAGCTGGTACAGATCTTTTATTACATATAAACTGGA
ATAAGCCATCTGTTCCAAGACAAAAGAGTAGGGCGAAAACAATACAAGAC
AGAAATGGAATTAGAACAAACCTGGGAGGAATGTGGAATTAGAGTAGAGA
GTCCAACACTGGCTGCAATCATAAAAATGTAAAACAAACAAAATTTGCT
AGGTGTGCTTACTTAGAAATAATTAGCTGTCTATTAAGTTCACTTGTGT
TATGGCTTAAATGTGTCCCCCAAATGTGATGTGTTGGAACTTGATCCC
CAATGCAACAGAGTTGAGAGATGGGACCTTTAAAGGTGATTAGGTCATA
AGGGTTCTGCCCTCATAAATGAATTAATACTGTTATCATGAGAGTAGATT
CCTGATAAAAGGATGATCTCTGCCTCCTCCCCACAGCCCTCTTGTGCATG
CTTTCCTGCCTTTCCACCTTCTGCTATGGGATGACACAGCAAGAAGGCCC
TCACCAAATGCAGCTCCTTGATCTTGGACTTTCCAGCCTCCAAAACCTGTA
AGCCAAACAAATTTCTGTTTATTATAAATTACCCAGTCTCAGGTATTCTG
TTCTAGAAACACAAAATGGACTAAGATCATTAATTAATCATTTTTTTATCA
GACTGTTGA

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AAAATATAACAGAGAGTAAGAGGAAAATTACCTTCTTTCTTTTCTTTTCT
CCTGCCTGACCTTATTCACCTCCCATCCCAGAGCATCCATTTATTCCATT
GATCTTTACTGACATCTATTATCTGACCTACACAATACTAGACATTAGGA
CAATGTGGCCTGCCTCCAAGAACTCAAATAAGCCAACTGAGATCAGAGA
GGATTAATCACCTGCCAATGGGCACAAAGCAACAAGCTGGGAGCCAAGTC
CCAAAATGGGGCCTGCTGCTTCCAGTTCCCTCTCTCTGCAATTGATGTC
GCATTATCCTTCGTCCCAGTCTGTCTCCACTACCACTTTCCCCCTCAAA

FIG. 3 (16 of 52)

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CACACACACACAACAGCCTTAGATGTTTTCTCCACTGATAAGTAGGTG
ACTCAATTTGTAAGTATATAATCCAAGACCTTCTATTCCTCAAGTAGAATT
TATGTGCCTGCCTGTGCTTTTCTACCTGGATCAAGTGATGTCTACAGAGT
AGGGCAGTAGCTTCATTCACTGAAGTCACTCAACAAGCATTATTTCACTGAG
AGCCTTGTATTTTTCAGGCATAGTGCCAACAGCAGTGTGGACAGTGGTG
ATCAAAGCCTCTAGTCTCATAGCAACTTAGTCTTCTGGAGGATATGGAAAA
CAGACAACCCAAACAACCAACAAAAGAGCAAGATGCTGCAAAAAAAAAA
AAATGAATAGGGTGCTAAGATAGAGAAAAGTGGGAGAGTGCTATTTAGAC
AAAGTGGTAAAAACAAGCCCCCTTGTGAGATGAGAGCTGCCGACAGGAGG
GGGCGGGTCATGGTTGTGGGTTTTTGGGTAGGACATTCAAGAGGAGGGGGC
GGGTCTGTGGTTGTGGGTTTTTGGGTAGGACATTCAAGAGGAGGGGGCGGGT
CGTGGTTGTGGGTTTTTGGGTAGGACATTCAAGAGGAGGGGGCGGGTCTGT
GTTGTGGGTTTTTGGGACATTCAAAAGAGTCTGAATGCACCCAGGCCCTAC
AACTTCAAGATGGTAAAGGACAGCTCCAAGGATCAGAAGAAGCATGCTTG
GAAGTGGGGCATTTTGAAGGAGGAAAAATATGCAGAGACTAGTGCTTG
CAGAGCTTGCATGTGGATTTCACTTGAGGTACAATGAAAACCCATTAATG
GGTTTCAACAGTGCATATGGCCTGACCTCACTTATATTTCTTAAATAGA
AAACAGATCAGAAGGAAGGCAATAGAGAAGCAGAAAGTCCAATGAGGAGG
TTTCAACAGCAGTCATGGGGTGGGGTAAGGAAAAGAAGTGGAAAGAAACA
GACAGAATTGGGTTATATTTTGGAGATAGAACCAACAGAAGGAAGAGGAG
AAACAACATTTACTGAGAAGGGAAAAAGTAGGAGAGGAATAGGTTTGGGA
AATAAATCCTGCTGACATTGGAACCCCAAGGAAGCCTCAAAAGTATATT
TACTTGCTTTAGATTTAAAAGAATAGGAAAGAAGCATCTCAACTTGGAAT
TTGAAATCTATTTTCCATAAAAGTATTGTTAAATCTACTCATACTCAC
AAGAAAAGTACATTCTAAAGAGTATATTGAAAGAGTTTACTGATATACTT
AGGAATTTTGTGTGTATGTGTGTGTGTGTGTATGCGTGTGTGTGTGTTAAC
CTTCAATTGTTGACTTAAATACTGAGATAAATGTCATCTAAATGCTAAAT
TGATTTCCCAAAGGTATGATTTGTTCACTTGGAGATCAAAATGTTTAGGG
GGCTTAGAATCACTGTAGTGCTCAGATTTGATGCAAAATGTCTTAGGCCCT
ATGTTGAAGGCAGGACAGAAACAATGTTTCCCTCCTACCTGCCTGGATAC
AGTAAGATACTAGTGTCACTGACAATCTTCATACTAATTTAGATCTCTC
TCCAATCACTAAGGAAATCACTCTTATTAATAGACTGGGCCACACATC
TACTAGGCATGTAATAAATGCTTGCTGAATGAACAAATGAATGAAGAGCC
TATAGCATCATGTTACAGCCATAGTCCTAAAGTGCTGTTTCTCATGAAGG
CCAAATGCTAAGGGATTGAGCTTCAGTCCTTTTTCTAACATCTTGTCTC
TAACAGAATCTCTTCTTTCTTCATAGGAGATGCCTGAGATACCCAAAA
CCATCACAGGTAGTGAGACCAACCTCCTCTTCTTCTGGGAACTCACGGC
ACTAAGAATCTATTTACATCAGTTGCCATCCAACTTGTTTATTGCCAC
AAAGCAAGACTACTGGGTGTGCTTGGCAGGGGGGCCACCCTCTATCACTG
ACTTTCAAGATACTGGAACCAAGGCGTAGGTCTGGAGTCTCACTTGTCTC
ACTTGTGCAGTGTTGACAGTTCATATGTACCATGTACATGAAGAAGCTAA
ATCCTTTACTGTTAGTCATTTGCTGAGCATGTANTGAGCCTTGTAATTCT
AAATGAATGTTTACACTCTTTGTAAGAGTGGAACCAACACTAACATATAA
TGTTGTTATTTAAAGAACACCCTATATTTTGCATAGTACCAATCATTTTA
ATTATTATCTTCATAACAATTTTAGGAGGACAGAGCTACTGACTATGG
CTACCAAAAAGACTCTACCCATATTACAGATGGGCAAATTAAGGCATAAG
AAAATAAGAAATATGCACAATAGCAGTTGAAACAAGAAGCCACAGACCT
AGGATTTTCATGATTTTCATTTCACTGTTTGCCTTCTACTTTTAAGTTGCT
GATGAACCTCTTAATCAAATAGCATAAGTTTCTGGGACCTCAGTTTATCA
TTTTCAAATGGAGGGAATAATACCTAAGCCTTCTGCGCAACAGTTTTT
TTATGCTAATCAGGGAGGTCATTTTGGTAAATACTTCTTGAAGCCGAGC
CTCAAGATGAAGGCAAGCACGAAATGTTATTTTTTAATTATTATTATA
TATGTATTTATAAATATATTTAAGATAATTATAATACTATATTATGG
GAACCCCTTCATCCTCTGAGTGTGACCAGGCATCCTCCACAATAGCAGAC
AGTGTCTTCTGGGATAAGTAAGTTTGATTTCAATTAACAGGGCATTTTG
GTCCAAGTTGTGCTTATCCCATAGCCAGGAACTCTGCATTCTAGTACTT
GGGAGACCTGTAATCATATAATAAATGTACATTAATTACCTTGAGCCAGT
AATTGGTCCGATCTTTGACTCTTTTGCCATTAACTTACCTGGGCATTCT
TGTTTCATTCAAATCCACCTGCAATCAAGTCCTACAAGCTAAAATTAGAT
GAACTCAACTTTGACAACCATGAGACCACTGTTATCAAACTTTCTTTTC

FIG. 3 (17 of 52)

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TGGAATGTAATCAATG1 . ICTTCTAGGTTCTAAAAATTGTGATCAGACCA
TAATGTTACATTATTATCAACAATAGTGATTGATAGAGTGTTCAGTCA
TAACTAAATAAAGCTTGCAACAAAATTCTCTGACACATAGTTATTCATTG
CCTTAATCATTATTTTACTGTCATGGTAATTAGGGACAAATGGTAAATGTT
TACATAAATAATTTGTATTTAGTGTACTTTATAAAATCAAACCAAGATTT
TATATTTTTTTCTCCTCTTTGTTAGCTGCCAGTATGCATAAATGGCATT
AGAATGATAATATTTCCGGGTTCACTTAAAGCTCACATTACACATACACA
AAACATGTGTTCCCATCTTTATACAAACTCACACATACAGAGCTACATTA
AAAACAATAATAGGCCAGGCACGGTGGCTCAGACCTGTAATCCAGCAC
TTTGGGAGGCCAAGGTGGGAAGATCACTTGAGGTCAGGAGTTCAAGACCA
GCCTAGGCAACATAGTGAGATCTCATCTCTACAAAAAAAATGAAAAAT
TAAAAATGAGCTGGACATGGTAGTACACACCTGTAGTCCCAGCTACTCG
GGAGGCTTGAGGTGGGAGGATCACTTGAGCCTGGGAGATGGAGGCTGCAG
TGAGCCATAATCACACCATTGCACCCCAACCTGGGCAACAGAGTGAGACC
CAGTCTCAAAAGATAAAATTTTAAAAATGTTAAAAATATATAAAAGAGA
ATTTTAAAGAACAATAATAGATCAAAGCATGGATGCAAGATATATTTA
GTTGGAATCAAGGTTAAAAATCAAGGGATCTTGGAATTAGGTGTGGTAG
ATTTGGGTAAGGAGTAGTCTAAGATGACCCTGTTTCTTGGTACTGGAGAC
TGGATGAGTGGCAGCGTCTTAACCATATTTTTGGTAGAAATATGGAGGTC
TTCTCCATTCCAGGATGAATGATGAGTAAATTTTAGGCATGTAATTTGA
GCTACTAGAAGGACACTCAATTGCAGATGTACAATGGGGAGATGATAACC
TATCTGGAACCTCAGAAAAATAACTGTATATAGATATGAAAGACATCAGTA
GGTATGTAGTAGATAAAATCCTAAAAGTGATGTCAAAGGGAGAAGAGAAG
TATATGGTGAACACTGTTGTTTGTCCATGCAATTGCCATCTCTTCTTCTT
CCTTACTGACAGAACCCTGATTTCACTGAGAAGTCAACATGCCCTTCCCC
AATTGATGAATCCAATTGGTTGAAGATTATGTTCAATTCTATTCTTACATG
ACTAAGTCACGTGTGACTTAATCCTATCAAATGAGATGTGATCTGGAAC
AACTTCTGGAAGATTTTCTACCTTGATAAAATAAGAGCCATATAGAT
GGTCTTTTATCTTCTTCTTCTTGAATGAGATATGTTCTATGAGGAAGT
GAAGCTTAGAACTGTGGTCAGCAACTTGCAACGACTGGGAAGTCAGAGCC
ACACAATGAAGAATGCAGAGTGGAAGGAGAAAAAGAGCCAGCATCTCTGA
CAACATTGTTACACCGAGAACCCTACCTCCAGATTTTAAGAAAACAAGAAA
TGCTACTGTTATTAAGCCATTTCACTGGGTTTGCTATGACTTGCAGTCAA
ATCTAGCTTAACTGATACAGAGCACCACAGAGAACTGGTCTCTCATTTGT
CTCATCTCTGTTCTTTCTAGCAGCCACGACTTTCCTAGGGTTTCTTAGCC
CAAGTCTGGCTAGAGCAAGACTAAGTAAGACTTGATTCCTTAATGTCCTT
TTGTTTTAAGAAATATTAAGAATTATTTTTATATTAATATATTTAAGA
ATAAGGAAATACAAAACACTGAGCAAGCAACACAAATTCAAGAAATCTT
AAAAAGTATAATAGCTGCTCAGTCTCTGATTAACAGTGAAATATGGAATC
ATTGTAGAAATGGCCTTGAGCGTTATTCTCCAGGCCAGCTATCCTTAT
GGTCTGCCCCACCTCCCTCATTGCCTAAACAGTAAGAGAGTCCCATGGTG
AGACTCAACAGTCTTAGCACAGAACTTGTTACAGTCTATTTCTTTCTTA
CAGTCTATATATCAATTCCAAATCAATGAGAGTAAAGCCCAATCCCTGC
CTTTAAACCCAAAGGACAGAAGCCCAAAGCCCAAAGATATTCCCTAACCT
TCTCCCCCT

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CCTGTCGCTCCCTATGTTTAAAGCTGGGGATCTCTTTTTCTGTGTCTAA
TTATTTTTCTCATTTGGCTTGAAAAATCTGATAAAACATTTTAGGACTGTG
TATAAATAGAATTAGCCAAGTGCAATGTCTTTATTCAGAAGAAATTTCA
TGGACGTTGTGCCTACTCTTGGCTTCTGGCTTCATGGCTTTCCAGAT
CCCACAGTAAGCTCTGGATAGTAGAAGTTATAGTAAGACTGACTTCTAAA
TAAATGAAGTGACTTTAACCTTACTGATATGGCTTAAAGAAAAGGAGTGG
CCTTTAAGATCCATGAACCTTCTCAAACAAAAGTGATAACGTTATCTCCAT
GCATATATAATACTAAATATAATGCAACTGAGAGAAGTAGGCTGTGGTAA
GAAAGGAGACCCAAGTGCCATCTGAAGGCAGCACTTACCCTCTGCTTCA
TCCCACCGAGGAAACAAAGCATGAGTATTGCCAGATTTTCTTCTGTTTCA
AGAAAGCCAGAAATCCAGGTTTTGCGTGAAATGTCCTGATTTTAAATGT
TGGGAACATAATTTATATTTTGAATAACATTGTGTGGGACAAGTGAACCT
GTATGTGGAACGTCTTTCTCCAGTGGCGACAGTTTGGACCGTTGATAC
TCAGCAAGTTCAGCCAAGTGCGCCTTGTCAATTGTCAAGTGTGAT

GTGTGATTGGTCAAACAATTAGTTTTGCTCAGCATCTCGTGTGTTTTCAA
AGGACCTGAGGGTTCAATTGCCCATGCAGATCTTGTAGTCCTGTTTTATTC
TATTAATTTATCTTGCAAATCTATAATGTTTTATTTTAAGCAGCGAGAGC
CGTGGCAGCCTTTGGTCTGGACCCTTTCTAATGATCATTTAGTATCAGGC
TATGTGGGAGTTGATTGTTTTGCATTGCCTGAAAGCCAACAGTATCACTC
CTCCTCTAGGTGTGGCAGAGATGTGAGAGAGGGAGACTGACAGTCTGTGG
GTGTGTATGCAGTGTGGGGGAAGCGAGGCACAGGGGACAATACTGTGGT
GTATAAACTAGTCTAAGGTAGCATCAGGAAGTTCATGAAGCCAAAATGA
TTTTTCATAACAGCACAAAGACATTATTTGTTTTTGCCTCCCTCTCATTTTT
TTTTTTTTTTGAGACAGAGTCTTGCTCTGTCTCATCCATGCTCGTGTGCAGT
GGTGCAATCTCGGCTCACTGCAACCTCCACCTCCAGGGTTCAAGCAATTC
TCATGCCTCAGCCTCCTGAGTAGCTGATTACAGGTCTGCACCACCCCGCC
GGCTAGTTTTTGTATTTTTAGTAGAGATGGGGTTTTGTAATGTTGGCCAG
GCTGCCCTGTCATTTTTTTTTACTAGTGTCCAGTGGAGTTTTTTAGGGG
CTACATAACATGATACTGTCAATTAATCTAATGGCTAATGAAAGGGATATG
TATATGTTTTTGTGTTTAAACAACCTCTTTGGGGTCCCTCAATAATTTT
TAAGAGTATAAAGGGTCCCTGAGATCAAAGAGTTTGAGTTCTGCTGGACT
GGGACAGTGGTTGTCAACCCAGATTGTACATTAGGGTCATCTGGGAAGCT
TTAAATAAGTACTGATGCCAACCTTACCGCAAACCAATTAAGCCAGAAT
CTCTGTGGATGAGAAGTCTTCATTGTCTCATCATCACCATGACCATCATCAT
TGTCACCGTCACTACACCATTATCATCATCATCATATCATCTTCATTATC
ATTGTTAGTATCTCCATCACCATCATCAGCATCACCATTATTATCATCAT
CATCATCCCCACCATCATCCTCATCGGAACCTCACCTGCATGGAGGACAA
TCCACTATGCATTAGGTGCTATGCTATTTGCTATACTCCTTATTCTCACA
ACTGCCCAGAGAGGCTGATATTATCTCACTTTATAACAGGAGGAATCTGG
ATCGGAAAAGTTAAGGTAAGCTAATTCACAGAGCGAGAAGAGATAGAGCC
AGGATTCGAAACCAGTTCTCTGCTACATCAATGTTCCAGTCCCTTGCACT
ATTGAGAACCTCTTTAGTTATGCTTTCACCCCTCCAACACCACAGTAAAT
TTTTTCTTTTTTAAAAAAATTATACTTTAAGTTATAGGGTATATGTGCA
TAATGTGCAGGTTTGTACATATGTATACATGTGCCATGTTGGTGTGCTG
CACTCATTAACCTCGTCATTTACATTAGGTATATCTTCTAATGCTATCCCT
CCCCGCTCTCCCCACCCCATGACAGGCCCTGGTGTGTGATGTTCCCCACC
CTGTGTCCAAGTGTCTCATTGTTCACTTCCCACCTATGAGTGAGAACAT
GTGGTGTGGTGTCTGTCTTGTGATAGTTTGCTCAGAATGATGGTTT
CCAGCTTCATCCACGTCCCTACAAAGGATATGAACTCATCCTTTTTTATG
GCTGCATAGTATTCCATGGTGTATGTGTGCCACATTTCTTAATCCAGTC
TATCATTTGCTGGACATTTGGGTGGTTCCAAGTCTTTGCTATTGTGAATA
GTGCCACAGTGAACATTTCATGTGCATGTGTCTTTATAGCAGCATGATTTA
TAATCCTTTGGGTATATACCCAGTAATGGGATGGCTGGGTCAAATGGTAT
TTCTAGTTCTAGATCCTTGAGGAATTGCCACACTGTCTACCACAATGGTT
GAATTAGTTTATAGCCCCACCAACAGTGTAAAGCATTCTTATTTCTCCA
CATCCTCTCCAGCACCTGTTGTTTCGTGACTTTTTAGTGATTGCCATTCT
AACTGGCACCACAGTAAATTTTTATAGATTTTATAAGCAAATTGTATTTA
CTGTGCAAGAATTGGTTTATTTTTTAAACCATGTGTTGCAAACATACAAT
GGTTAATTGTGATATTTGCTCAGTACAAGATCATCAGATCACTACACAGA
CTTGAGGTAATTCACCTAAAAGCAAAGAGAACTGACCCCACTTAAGT
AGAAGTCTTTACTTATTTATTCCTATAAAGCAGCCAATATGAAGAGAAG
GCCTTAATGTGGTTAACTATGTAATTTTTTTCTGACTTTTTGAAATACTG
AGAAGAGCTCATGACTCTCCCATCTCCTAATTCTACCTTGGTGGATTTTA
GACTGACCACAACCTCATGGGTAAATGAGGGAAGACGAATAAGAAACCTTG
CTTTTTTTCTCCTTGTGTTTTGGCTGGCTGCAGTGGCTCACACCTGTAA
TCTCATCACTTTGGGAGGCCAAGGTGGGAAGATCACTTGAGCTCAGGATT
TCAAAACTGGCCTGGGCAACATAGTGAGACCCCATCTCTAAAAA
AAAAAAAAAAGGCGACAGGCGGTGCGTGCTGTAATCCTACCTACTC
AAGAAGCCGAGGTGGAAAGATCACTTGAGCATGGGAGGTCAAAGCTGCAG
TGAACCTTGATTGCACCACTTCATTCCAGCCTGGGTGACAAAGCAGGACG
CTGCCTCAAGAAAACAAAAACAAACCTTAATTTTTTGGCTATTCTTTTC
TGGTAAGAATGGTATAGAGATGGGGATGAGGATGGCTATTGTATGAGAGA
GCAAACAGGGTCCAAGCAGTGCTCTGGGCTGTCTAAGGACCAGTAGTCAG
CTTAACCTCTCAAATTTCCAGGGAAGGAGTTCGGAGTGGTAGAATATCCT

FIG. 3 (19 of 52)

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GGGTATGCCCAAAGCATCACCTTGCAAATAGCCTGTGATGAATAATTTG
TTCATTTGTTATGACTGGAACTGGCTTTGTGTATGCCAGAGAATGGGGG
CAGGAAAGAGAGATTGGTGTCTTGAGCTCTCTGTGCCTCTGGGGCAGTGA
TGCTTTTCTCTCATGTGGAAGGAGAGCATGACTGAAAAGGTGCACAAAT
AAGGTGTCTGTGAGAGAAATTAACCTTCCAGATACAGAGACACAACCTTC
CCCAAGAGGTCTCATTGCTCTGCCTTTTTTCCTTTTTTTTGTCTGTTCT
AQCATTAAATAACAGAACTGATTATGACCTCAAAGAGAGAGAAAGCGA
CTCTCCCCACCCTAGAGCTAGTTAACCACCATATCTTCCTAGATATCCTT
GAGAGCAATGTAACCC

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GTGAACCTGTTTTACCTGTGTAGCAGACCAAGCCGAGACAAAATCCNTC
AGACACCAAATTAAGAAGGAAGGGCTTTATTGGGCCTGGAGCTGCGGCA
AGACTCACGTCTCCAACAACCGAGCTCCCCGAGTGTGCAATTCCTGTCCC
TTTTAAGGGCTCACAACCTTAAGGCGGTCCACATGAGAGAGTCGTGATAG
ATTGAGCAAGCAGGGGTATGTGACTGGGGGCTGCATGCACCTGTAGTTA
GAATGGAACAGAACATGACAGGGATCTTCACAGTGTCTTTCTATGCAAA
TAACCGATTAGATCAGGGGTGATCTTTACCAGGGCCAGGGTGTGTCAAC
GGCTGTCTGCTGTGGATTTCATTTCTGCCTTTTAGTTATTACTTCTTT
CTTTGGAGGCAGAAATTGGGCATAAGACAATATGAGGGGTGGTCTCCTCT
CTTACCTGCGGGGAGTGAGCTCAAACCTCTTAAAGGAGTTACCTGCCTTC
CATCATCAGGGAAGCAGGAAATCTTGCTTCCTTGTGGAAGCAAGTAAA
ACTCAAAACAAACAAAGAAAAAACAGGGAGTTGTACAGCAAAATAAACT
TTTGATTTTGACCAAATTTTGGGAGATCAGGAATTCTCTGAAGGAGATGC
TTTCAGACCTCAGCAAATTGTCTGTTGGTTTGAGCCATAAAGTTAGCTC
ATGCTGGTACCAAACACCAGTAGGAGATTTGTCAAAGGTAAGAGGCATCT
CCACTCAGAATCCCTTCGTGGTTACCAACATGTGAACCTTGGAATCTGA
GACAGGTCTCAGTTAATTTAGAAAGTTTATTTTGCCACGGTTGAGGACAC
GCACCCATGACAGGCATCAGGAGGTCTTGACCACATGTGCTCAGGGTGG
TCTGAGCAGCTTGGTTTTACACATTTTAGGGAGACATGAGACATCAGT
GAATATATGTAAGATGTACACTGGTTCCCTCCAGAAAGGCAGAACAACTT
GAAGCAGGGAGGGAGCTTCCAGGTCACAGGTAGGTGAGAGACAAACAATT
GCATTCTTCTGAGTGTCTGATTAGCCTTTCCAAGGAGGCAATCAGATAT
GCATTTATCACAGTGAGCAGAGGGGTGACTTTGAATAGAATGGGAGGCAG
GTTTGCCCTAAGCAGTTCCAGCTTGACTTTTCCCTTTAGCTTAGTGATT
TGGAGGCCCAAGATTTATTTCTCTTCTACATCACTGTGGGCAGCTGACT
AGGAAAGCTTTGTAGGACTGGTGGGCAGTGTGAGAGCCCAGTGGGGGGTG
GTGGTCTGTGCCAATGGTAGCAACCACCTGTGAGGCTGAGTAACTCAT
TTCCCAACCTCCTCTAGCAGCCCCAGTGAGATACAGAGGAAGCAGACTA
GCGATACAACCCAGCTGAAGTTTTGTCTGGTGAGTGAATGAATAAAA
ATGGGAAGGGTGCTGAAGAGACCAGCAAGAAAATGGTTGAAGAGATGGGG
CACAGAAATTAAGCTGGATCAAAAAGGACGGAAAAGCAGAAAGGGCCGAT
AGAGAGAGGGGATATCTATGGGTTCGCGATTCTGAAAAGGACAAATCACT
GGTGCTTTGAGAAGAGAGAGGGTGAGAAAGCAGGAAGGCTGGAGGCTGTC
ATCCAAGAGGCGGACATCTGTGAACATGATTCCAAGAGTCACCAGACCAT
GGGGGTGGCCAAAGGGAGTGCCTCTTCTCACTCTCTACTCTTAATTCCTT
GTACTCAAGATAATAAGTTCCAGAAAGAGAAGTACCCATATTTAATTCAT
CTGTGTCTTCTAGCAGTACTAAAAATATTATATGAAAGGTATCAAACCT
TTGAGAATGTGTGCTGTAAATTGTTAAGGATGCTGGAAAACCTCAAGACG
TCCCTGATCCTGAGCTGAGTATGAGCCTGTGGTGAGCCCAATGCAGGTCT
TCCATTGAGACAAAGGCCTCAGGGAACGGATGAGACCTAGGGACAGAGAT
GCATGCTGGAGCAGCATTCCCCATCCCTACTGCAGCTCAGGCCAGCTGAC
TGCTTTATGAGTAAACGTTACCAGGGAACACTTTGCAGTCTTAACACACA
TGCCACCTGTGACCACTGATCCCTGTTGGGTGACCACTGACATCAGAGA
TTCGATGGCAGCAATGAAGACAAGGCTATCCTCATTAGGAAGGAAAGGAA
GGAGGAGGGAGGAGGGCAAACGAATCTTTCCTGCTTGTCAACCACGTCCA
TCTCTGTTAGGTGATTTCCCATGTGTGACTTTGTTTATCTTTATAATAAC
TCTGAGAGGTAGGTCTTGATGTCCACATTTTGAACATGAGGACATCCAGC
CAGGAAGTTGAGTTCTGGGGACATAGCTGAGAGGGCAAAGCTACATATAA
ACCCCTCTTTGTTTTTCTGGCTTATCCACTGAGTGCCCCCTGCAATCCA
CCAGCCCATTTGTGAAGTGCTACTATAGGTAAAGTTGGCACAGGAGGAGT

GGATGTGGGCGATTTTG. CACAGCTCTCCAGGAACTTACACACTGGTGAG
GAGGGCCAGGTATGTTCCCTGACCAGTCACAATCAAAGCAACCTCCTACTA
ATCAGGGAGGCTTGGTACCTGGGGAATGCTATGTTGAAAGGTTCTTTTCT
GGGTTTTAAATGATGGGTCTATTTCCTTATTCTTAAGATTGCTTTTTT
CTGGCTAGAACTTAAAAGAAATTTTCAGTAAATTTCCCTTCCCTGGCAC
AAAGTGAGCTTGAAATGAATTCAGGTGGCCTTGATACTTTAAATATT
GCCTCCTATAAAATCAACCTTTAGAAGAAGGAAGTCAAAGAACATGCTAG
ATTTCAAAAGGTTAATTCCTTGAAATCCAGTTATCTACAGGACAATGTT
GTCAAAGAAAAAATTATTTGGCCAGGCACGGCGGCTCATGCCTATAATCC
CAGCACTTTGGGAGGCTGAGGCAGGTGATCACCTGAGGTCAGGAGTTCGA
GACCAGCCTGGCCAACATGGTGAAACCCCATCTCTACTAAAAATACAAAA
AAAATTAGCCAGGTGTGGTGGTGGGCACCTGTAATCCAGCTACACGGGA
GGCTGAGGCAGGAGAATCGCTTGAAACCCGGGAGGAGGAAGTTGCAGTGAG
CCAAGTTCAAGCCACTGCACCCAGCCTGGGCAACAGAGCAAGACTTTGT
CTCCAAAAAATAAATCAATGATATTTTAAATTCATGGTAAGGAA
GATTTCAATTCAGAACCAGCACAGAAGATATAGGAAACACTGCAATGGGAC
TTTGCGGTGGGGGAGAGAGATTGAACACAACACTACATATACAGCACGGGCA
AGGACATATTCATAGCCAGGAAGCAGAGCAAAGATCAGTGGATGCGAAAT
TACTAAGAGGAAACATGAAAAATAAGGGAGCTTCTGCCTAAACCCACCTA
ACCGGATCCTTGCTGAAGACAGGACAGGGTGATTGGACACCACTTTGGGG
ATGGTGGAGGATGGGGAATCCAGTGAGATTTCAAGGGTGATGCGAFATTG
AACATACAAAGTTCTTGCTAAAAAAGGATTTTACAAGAAAGTGACAAAT
GTGCCTGGGACAAGGTGCAGGAGCCCGACGGAGATGTGGTCCAGCAGAGA
ATATGTGCCGAGATGATAGGTGAGTTCTCTGACGAAGGATATATGCTGAT
CCAGCCAGGGTGAAATGCTCAGAGAAAGCACGGAGGGGCTATGTCCGTTG
CCCCAGTCTCCACGCGGTCAAATCTGATCCCGTTGTGAGTGTGGCCGTTT
GTAGAAAGCAATCAGGGGGGTCCTCCTCCCC

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AATATATATTTTTTATANNATNTGAGACAGGTTCTCACTAGGTTGCCCAG
GCTGGTCTTGAATTCCTGCCTTCAAGTGACTCTCCACCTTAGCCTACTG
CATAGCTGGGATTACAGGCACAAACCACTGCATGCAGCTAACTTTGCTTC
TCATTCCAGCACTTTTTATTCCACTGATTATATGTATATGTATATCTGCA
TCATCTCTCTCTCTCTCTCTCTCTCTCTCTCTATATATATATATATAT
ATGGAAATATCTCTCTCTCTCTCTATATATATATATGGAATATATATCT
CAGTCTCTCCTATCCTCCTTTAATCAGTTTTGCTATCCTGTCAATTCCCC
CAACGAGTGTGATGTTGTGAAATATATATTTGTTCTTCATCTCCTGTTTC
CTGACATACAGCTTTTAAAAACCCTTGGAATCTCTGGAATAATAAGAGTG
TCTTTTGCACTGCTAATAGATGACTGCTGGCTGGCAGCCCCAATGCAGTAG
CTTCATGATGGGGTTTTGTACAGGAAAGACCAAGGCAGGATTGGAGACTT
GAGACTGTTAGCCCCACTCCCCAACCCTGGAGGGAGTGGAGGGGCTGAA
GGTTGTGTGTCAGTCACCAATGGCCAATGGTTCGGTCAATCATGTGTATGTA
ATAAAGCCACTCTTAAAAACCCAAAAGGACAGGGTTTGGAAGGGCTCCC
AGATAGCTGGACACATGAAGGTTCTTGAGGGTGGTGCCCCAGAGGGGCA
TGGAAGCTCCACACCCCTTCTCACATGCTTTGCTCTGCGCATCTCTTCAT
CTGGTGTTCATCTGTATCCTTTGTAATATCTTTTAGAATAAACTGGTAAA
CTTAAGTGTTTTCTGAGTTCTGTGAGCTGCTCTAGCAAATTCACGGAAC
CCGAGGGAAGCAAACCCAGATTTATAGCCATCAGTCAGAAGCATAGGTGA
CAACCTACCACTTGTAACTGGCACCTGAAGTGGGAGGCAGTCTTGTGAGA
CTGAGCCCTCAACCTGTGGGATCTAACGCTAACTCCAGGTAGATAGTGT
GGAGTGAATTAGGACACCCAACTGGTGTGCGGCTGCTGGAGGACTAGTGGT
GGGAGAAATCCCCAAGCATTTCCGGTGAAGTACAGAGGTACAGAAGAACTCAG
TGTTGAGGTGTTGTGACAGTATGGTAGGGAAAAGTGCCTGCTGGTTTTTTC
CTTTTACAATCAGTTAAATATTTAACACAAGTCTACTGTATATTAGTAAA
AGGGTTACATTTTTTAAATGTCTTGACAGTTGCACTTTGACAACCTCCATA
TCAATCACTTTTTTTCGTGTCCGTTTGGAACCAAATCACTTGGGATACC
ATGAACCAGGCTGCAGCGTATTCCTCCAGGCCTTGAAAGCTTGAGGGCCAT
TTTGCCAGCCNTAATCCCTGTGAATACCAGGCTTCGTGGATTTAAAAAT
AGACTTGAGGCCAGGCCTGGTGGCTCACACCTGTAAGCCCAGCACTTTGG
GAGGTCAGGGCGGATAGATCAAGGTTAGGAGTTCGAGACCAGCGTGGC
CAACATGGTGAAACCCGCTCTCTACTAAATATACAAAAAATAAGCCG

GGCGTGATGTTACACG...AGTAGTGCCAGATACTCAGGAGGCTGAGGCGAG
GAGAAATACTTGAACCTGGGAGGCAGAGGTTGAAATGAGTCAAGATCGTG
CCACTGCACTCCAGCTTGGGCGACAGAGTGAGACTCAGTTTTTCAGGGGAG
TTAAACAATAACAAAAAAGAAAAAGACTTGAACAATGAGGCTCCACTGG
ATGGATTTAGGGGAATTACAGGAAGCAGGACCTGACGGTGCAATGCCACA
CTCCACCTGTCCAGAATTGGACCTCACCAAGGGAGGTCTGTGGGGACAGG
GAGAGGCCCTCTGCCTCCACCCCTCCTCTACTCCCCAAACCCTGAGTCA
GGCTGAATGTAGTAAACCTGGAACAGAAAAGTTTCAAGTTTGGCAATAGGTA
TCTGAAGGACTCCAGGTGCTTCTCCCTTGATTCAAAATTTTACTTATAAA
AAAAATTATAAGAAAATTCTACTTAAAAGAAATAATCAGGGAGGTACAAC
AAATTGTACTTTTTTTTTTTTTTTTTTTTTTTTGAATGGAGTCTCACTG
TTGCCCATGCTGGAGTACAGTAGTGTGATCTCGGCTCACTGCAACCTCCG
CCTCCTAGGTTCAAGTGATTTTCTACTTCAGCCTCCCAAGTAGCTGCGA
TTACAGGTGTGTGCCACCACACCCGGCTAATTTTTGTATTTTTTGGTAGAG
ACGGGTTTTACCATGTTAACCAAGATGGTCTCGAACTCCTGACCTCAGG
TGACCCACCTGCCTCAGACTCCCAAAGTGTGGGATTACAGGGGTGAGCC
ACTAAGCCCAGCCATTGTACATATTTTGTGGGTATTTACTAAAACATTAT
TCAAAATAGTAAAAAAAATTGAAATAAACTGGGGACTGGTTAAATAATT
TTGGGTACAACCACATGATGGAATACTATACAGCCATTAAAAATTACATT
GAGGCCAGGTGTGGTGGCTCATGCTTGTAACTTAGCACTTTGGGAGGCC
AAAGTGGGAGGATTGCTTGGACCCAGGAGCTCAAGACCAGCTTGGGCAAT
GTGGCAAAACCCTGTCTCTAAAAAAAATAACAAAAAATTAAAAAGCT
GGGTGTGGAGGCACACACCTCTAGTCCCAGCTACTCAAAGGGCTAAGGTG
GGAAGATCACTTGAACCGGGGAGGTCAAGGCTGCAGTGACCCAAAATCGG
GTCAATTGCACTCCAGCCTGGGCAACAAAGCAAGACCCTGTCTCAAAAAA
AAAAAATAATGAAGATACTTACGGTATGGATAAATATTCAATTTTA
CAGTGATAGATGCAAATAAAAGCAAATTACAAAATATACAGTTTAATTCC
AACTTTGATACTACATATGTATATATGAATACATGCATATGTTATGTATG
TATATGTAAATATAACAATATATGTTCTATATATGGATATTATATATTTA
CACATACATACACATATATAATATCTTCTCTAGAGAGCAGAAAGAGAG
TAGACAGATAATGAAGATAGGATACAACCTCCAGTCCAGCTCAACCTAGGG
GACTTGTTTTAAAGCCTCAGGAGAGAGAAGTTGGGACTAGAAAGCAAGGC
AGCTATTTGTAAAGCATCTTTGTGTTTCATGCTATTGGGGTGGGAAACAAC
AGCACAACCTTTTGAAGCCCCCTTCTACTCACCCACAACTGCAGAGCA
GCTTTAGGACCCCTCAGAGTTCAAGAAGACCATTGTCAGAGTAGAAGAAGT
AAAAAATGATGAACCTTGACCCTGAGCTCATGGACTGTGCCATGAGGGA
AATTCTTAAGACGAGGAGAGGCCCTGGAGGAAGGCAGAGGCCCTGCAT
CAGCAAGTCCAGGCAAAAGCCTGCATTCCATAGATGCTCATCTCTCTGGC
TGGTGAGGTCTAAAGACGTTTGGTCTCAATATTAAGTCTCGTGAGAGAGG
TCACAAACCAGTCCCTTGGCCACAAAGGAAATAAATTCTGGCTTGAGA
CATTAGGGAGGAACAGGGCAAGGGGAGGTTCAAGAAAGTTTTAATGGATG
AGATGATATTTAAGCAAGGCCCTGGAAAATGAGAATTTCAACCAATAGCC
ATATGGTAGGTGAGAAAGCAAGATAAGGAGGGGGCAAGTGCAAGGGGCA
ACATCAGATATGACCAGGGTGTCTGTTGGGTCATGGCTGATGGAGAAGAAGA
TTAGACTGGAGTTTGGGAATGCCACAGTATCGAGGTTGGATTTAATCCTA
TGGGTAATAAAGCCAACTGTTCAACCCCCAACCCACTTGCAATATGGCTC
CAAAATAGCAGGTGTTTGATAAAATGACTACTTTTACTCTACTATTCCCT
CCCTCTTAAGAAGAAAAAGAAAGTGGAGGCTCAGAGAAAGGCAGTGGCTT
GTCCCAATCACACTATGATTTGGCCACAAAACAAGAACGAAATGTTACAC
CCAAAAATGCTGCCTCCACCTCCCTTCTTGTCTTCTCCTCCTGCTGGACT
ACAGACTATCTCAAGAGTGACGTACACCATCAGGGCTTCAGCTTTTCCCC
GAAACAATGCCAAAATATTAGCCATACGTCACTGTAGTAAGAGCCCTGAA
TTGGGAATCCCAGCTTTGACGCAGACATGCTGATTGACTCTGTGACCATT
CTCTTCACTTCTCCACTCTATTCTTCCCCACCTGTAAAGTGAGGTCCTTT
CCAGTTATAAAAAACAGATGATGCTATTGTCTGTTTTGTATCTAATCTTG
CTGTGTTATAAAAAAAAATAAGGCTCTGTACATTCATCTTGGCCAATTC
CCTTCTTATCTACTTCCCCACAGCCCCTTTTCTACAGAAAACCAGCAT
TGTTCTTCTGGATCCATCTCTTAAGAAAGCGCTTTGCCTCCCCGGTTATT
TAGGTGATAAGAAGTGTCTAGATGACAGCCCTGGAATGGGCTGGAGGCA
ACAAAAAGCAAGTGAATAGACAGTTACAGCGACGACAATAATAACAAC

FIG. 3 (22 of 52)

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CAACACCTCTCACTAAAGAGAAAGAAATAAAAAAGAAAATTAAAAATCTGC
CGCAATGCCCACACAGTCATTGAATAACTGCATGTGTACAGCACTTGGTT
ACTTTTACATACTTCATATTTTAGCCTTCATAGCAGCTCACAGGGGTGGA
TTTAATTTTTAGTCCAACCTCCTGTCACGGTGCCTGGCACAAGTATAATA
ATGTTCTGTGAATAAATGACCCCTTTTTTAGATGAGGAAATCGAGGCTCA
AGGAGAACAAGCAATGTAATGTCCCCCTCCTGTTGAGCCATCTGCCTTTC
ACGCCACTGAATGCAGTAGTCCTCAGTGCCCTGAACTTGACCCCTCTCTG
CTTTTCGGACTGGTCCTTCTAATCCCCGTTGTGACTCACTACACCACCTCT
CCTGCATATGACATCTACATTTTAAAAACAAACCGTATGGAAATAACACAT
TAGTCGGCTTGTTCCTCCCCACCCCGCAAAAAAAGGCCCTCTTTATAACA
GAAACTTCTCAGGCTGGTAGGGGAATTTTATTCCCCCATTATGGTAGAA
AGGCCCTAACCTTGACCTCAGCCATAGCTATTACATGGGGGAATGAT
GAATAACATGGGGAGCAGCATGTAAATATCATTGAGCCGTAGTCCAGACC
TATAACACATC

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GGGGGAGCTGCATGTGCCTGTGCGAGATCTGGGGGAGGAACAGGAAGATCA
AGAGTTCTGTGTAGGACATGTTAAGTTGAAGGTGCTTACAGGATAGCCAG
ATGAAGCATCAGGTGTGCAGTCAAAGATATGAGTCTGGAGCAGCACATCC
TAAGTCACCTCCTGCACCAACACAGAACTTCCAGGCCACTCACTTGAGCT
CTCCCAAATAGATTTCCAAGTGTCTATTATGTTAATAACCTATGAGCTTGAA
CACCAGATTCAAACCCCACTGCATGGCTTTTAAAGACCATCTCAAGGGCT
TGACACTCCAGGGAGCCAACTAAAGATGCCTGGTCTTACCATCAACCTCC
ACCCCATTTTTTATAGAAAATGTTTCTACCTGTCTTAAGGCAGGGTCTTG
CCCCACTCCAGGCCCTTTAGATCCCCAATATTCTCTCTCCCTGAACCA
AAACCTCATCATCTTCCAGCATGGGTGGGGCCTCCATTCTTGCTTCTGC
TCCCTGAGCAGAAGCAAGTTTCTCCCAACTTGACCTGATTCTCTCTCTA
AGTACCAGTCACTGCTTTGTTTCTGGAATGAGAGAAAAAGACAGAGTGAG
AGAGACAATCCAGAACTCTTGCTCACTCACAGCTAGGCTGGGCATCTGGG
AGGATGGCTGTGTCCATGGGAACCTGGGAAAAGCCACACCCTTGGCACCC
TGGTCACCCACCTGTCTCCCTGGCAGATTCCGCACTGCTCTCTTGACCC
TCTACCCAGGGCTAACCGGCCTGCTCACTCTCCCCAGCATGTCTTCCACG
CCCCTCTCTAATTATTACATTCCCTTACATAAACTGCCCTTCTCTCCC
AATCACCACATGTTCACTTCCCACCCAGCTGTCAAAGTCTGGCTCAACCT
CATCTTGAAAAGGAAAAACAAACAAACAAACAAACAAACAAAGCAAAAA
ACCTATGATGGATTAAGAACACACTTCATTCCAGGAACATGCTTATCTCC
TCTAACTCTCACAACAACTACAGCAGGTAGGTGTTATCACACCCATCTCT
CAGGTGAGAAAAACAGGCTCAACGAGTGCAGGAGGACACAGCAAGTCAGTG
ACAAAGCTTAAATTCAAGCCCAAGCCTGTTGGCAACCAACGTCTGTACCC
TTGATAGCTACCTCATTTACCACCAAATCCAGTGGCCTCAGGCCTGGCTG
CACACTGGGATCACCTGGTGGCCAGACCACATCTTAGACCAGTCATACAG
AATCTCTTGGGCTGGGATCCTCCACGGTACATTTTAAGGGTCCCAGGTG
AGTTCACCATGGAACCCAGAATTGAGGACCAATACCGTATACCATCTCC
TTCTTCATCTCTTCTAAGGCATCTCTTACTCGCTGTGCACTCCCATACCA
CTTTGTTCAATCATCCAATCATTCACTTCACTGAGTCAGTTAGTCAGGAGC
TACTCACTAGTCCCCTGCCAGGTCTAGTCATGACATAGGGCTCTGGGGA
CCAACAAGAAGCAGGACCCATGCCTCCTGCTCTCATGGAGCTTGCTCTGC
AGCAGAGGAAGCAGTCAGTGAGATGTAGCAAATGTGAAATGTGCACAGAT
GGGAAAAGCAAACTTTAAACTTTTAGGACAAAATACACAAGAAATCTT
TGCAACTTTGGGACAGGAAGGAACAACATTCCTTACACATGACACCAAAG
GAATCAACCATAAAATAAAAAGGTGATCAATTTGACCTCATTTAAGTGTTA
AGCTTTTTTCAATTGAGAGACACCATTAATAAATTAATAATACATGCCACAA
ACTGGGATACAAATTATTAACACTTATGTCTCACAAGGATTAGTTTTTC
AGAATATATAAAGAAGTCCCGCCGGGTATGGCCGCGCAGCTGGAATCT
CAGCACTTTGGGAGGCCAGCGGATCACATGAGGTGAGGATTCAAGACCA
GCCTGGCCAACATGGCAAACTCCGTCTCTACTAAAAATACAAAAATTAG
CCAGGCATGGTGGCGGGCGCCTGTAATCCAGCTACTCAGGAACTGAGG
CAGGAGAATCACTTGAGCCCAGAAAACAGAAGTTGCAGTGAGCTGAGCTC
ACATCACTGTAAGCCTCGGTGACAGAGTAAGACTGTCAAAAAACGAAAA
CAAAAAACAAAACCTCTACAAATAAATAAGAAAAAATAGCCAGCAGGA
AAAAGTATATACATTTCTAATAAAGATAAATACATTCTGTCAGTTTTCTA

FIG. 3 (23 of 52)

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ACATATATTTTTTAAGAGTAAATACAAATGGTTAGGAAACATTTTTTAA
ATGCCCAACCTCATTAAAAATTATAGAAGTGAAATTAAGCCACAATAAG
ATACGATTTTATACCAAATACAGTGTCAACACTTTGCAAGTCTGACCTCA
CCAAGTGTACCAGACGTGTGCACTGACGTGGCTGCTGAGATACTGATGG
TGGGTCTGTAAATCTGTACTACAAACAATTGCAATAAAATGTAATAAATA
TACAATAGGTGGAGCAGGAAGTGACCTGCAACCATATAGCAGATAGGGCA
GGAAAAAGCCTATGAAAGCTGACATCAAAGGGATAAGTTCCAGTTACCCA
GCTGAAGGGAAGGAGGGTGTTCAGATAGAGGAAGGATAAGCATGACCTA
TTCAAGGCCAGTGAAAGAAGCGTGCAACGGCCAAGTCAGGAGAACCTGAA
ATTGTGTCAAAGAGCTTGGATGCAAAGAGCCGTGGGAGACTATTGGGGGT
TTTAAGCAGGGATATAATATTTCATTCAAGCATGCAGTAAAAGGTCAGTGG
CACCTGCCATGGGCCAGGACTCGGGCTCTACATGATTGCGTCTGTTTTGG
AAATATCACCTGGCTGTGAGATGAAGAACAGGTAGGAGGGTCACAAAAC
TTGAAGCAGAGAGACTGTTGAGGAAGTAAGCTGTTTTTGTGTGGACTGTG
GCAATCACAGAGGCAGAGGATATAAATGCACAGAGACACAAGGCATGTGG
GAGGCAGAAGGAATCAAATACAATGAGTGATCAGATGTGGGGTTAGAGTG
GTGAGTGAGAAGACATACTCAAGGTGACACGCCAGGTATCTGGGTGGAT
GGTAAGACATTCATGGACTAGGATCGAGGAANGAGGTGGGGAATGGGACC
ATACCTGCAGTTTATAAGGGGTGGACGAGGGAAGATTATGCGGGAGACTG
AGAGAGGAATAGACAAAGGAATCCCGGTGCAGTATTACAGAACTGGGGT
GGGAGGGGGTTGTANTTCAAAAAGGAAAGAAAATTGTCAAATAGTATGAA
ATGCTGCAGAGAAACTCACGGATTTTTTTTTTAAGCTTAGAATTATTCAT
TGACTATGTGAATAAGAATAACTTTTATGAAAGAAGTTTTGCTTAAGTAG
TAGGAAGAAGCAAAATTGTTGAGGGCTGATGAGTGGGAGGAGAAGTAATT
GAAGGCACCTCTTCAAGAGAAACAAAGCAGAAGGTGAGGAGAATACTAAT
GAAGGAGTTACGGCCTTCACTATTTTGTGTTTTGCTTTAGATAAGCAAGACT
TGAGTGGGTCTGGTGAGGAGAAACAAGTAGAGTACAAAGTTAAAGGAGAG
ACAGACAGAGATAGAGATAGGGACAGAGAGAGAGACAGAGACAGAGCACA
AAAGAGCAAGGTCCCTGAGAACACGGGCCTTCTGTTTAAACCCCAGCCAG
ATGTATTGCAATTCAATTCCAGTACTAACCACCCAGAGTTTGTGTAGACT
CTACAGGTTAAAGAGCATGGTCCCCAACAAGACTGCTTCTACGTCAGATG
CCAGGCACATTCAGGGGTCCCCAAGCCACTCATGTTTTTTGAATGACTG
CCATAAGTTCAAAAATTCCCACAATTCTCTCAGATTCAATAACTGGGTAT
AACCACCTCATAGAACTCAAGAAAATGCTATCATTATTATTACAATTTTAT
TATAAAGGATACAAATCAGAAGGACTAGCCAAATGAGGAGACACATAGAG
AGAGGACTAGTAAAAACAGAGCTTCTGCGTCTACCTTCAAGGAATCAG
GATGCACCAACCTCCCAGCACATCAAGTGCTCATCAACCAGGAAGTTCCT
CTGAGCTCCAATGTCCAGAGATTTTAGGGAGGATTCATTACATAGGTATC
ATTGATTAAATCATTGGCCATGTACTTGAATCAATCTCCAGTGTCCCTC
TTCTCCCTAGAGGTCTGAAGGGTTGGCTAATATCATGTGGCTCAAAGCCC
CAACTCTAATTACCTTTTTGGTCTTTTCAGGGACTAGACCCCATCTGAA
GCTATCTACAGGCCCTGCCATGAGTTAGCTCATTAAACATAACAAAGACAC
TTATATTACTCAGAAAATTCCAACAGTTTTTAGAAGCTCCATGTCAGGAAC
CTGGGACATAGATCAAATTCTTTTTTTTTTTTTTTTTTTTGGAGACAGGGT
CTTGCTGTGTTGCCAGGCTAGAGTGCAACGACAGATCACAGCTCAATGC
AGCTTCAACTTCCCAGGCTTAAGTGACCTTCCACCTTAACCTTCCAAGT
ATCTGGGACCACAGAAAATGGCTAATTATCCTGGCTGATTTTTAACTTT
TTTTTTTTGTAGGGATGGGATCGCCCTGTGTTGCCAAGGTTGGTCTCAA
CTCCTGGGTTCAAGCAATCATTCTGCCCTGGCCTCTGTGATGGTTAATAC
TGAGTGTCAACTTGATTGGATTGAAGGATACAAAGTATTATTTTTGGGTG
TGTCTGTGAGGGTGTGGCCAAAGGAGATTACATTTGAGTCAGTGGACTGG
GAAAGTCCACCTTTCCAGTGGACTGGGAGACCCACCTCAATCCAGGT
AAACACAATCTAATCAGCTGCCAGTGTGGTCAGAATAAAAGGAGGCAGAA
GAACAGGGAAACACTAGACTGGCTTAGTCTTCCAGCCTACATCTTCTCT
CATGCTGAATGCTTCTACCTCGAACATCAGCCTCCAAGTTCTTCAGTT
TTTGGACTCTTGACCTTCAACCACAGATTGAAGACTGCAGTGTGGCTT
CCCTGTTTTTGGAGTTTTGGGACTCAGACTGGCTTCTTGCTCCTCAGCT
TGCAGATGGCCAATTGTGGGACTTTAACTTGTGATCATGTGAGTCAATAT
TCCTTAATAAACTCAGATATATATATATGTATCAGACATATATATATATC
CTATTGTATATTATATACAGATATATAATATCCTATTATATACAGATATA

FIG. 3 (24 of 52)

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TAATATCCTATTATATACAGGTATATATATATATATGTATCATATATAIA
TATCCTATTGGTTCTATCCCTCTTGAGAATCCTGACTAATACAGCCTCCC
AAAATGCTGAGATTACAGGAGTGAGCCACAGCCACCATGCCAGCCCCAA
ATTCTTAATTATACAACAATGGGTCCAGAGATCAGGGCCTGGGTAGGATG
CAGCAATAAGAAAACAGATGGTGGATGGGGACACATGTTGGAAGTGTGGC
AGGACATGGCTGAGGGAACCTCATAGGATGGTGTCTATTTTCATGGCTGAG
TGTGAGGAACAGCATAAGGTCAAAATTTTCAGGTCAATGGTGAGTTTTTTA
AATTGTTGCTGTGAACCCCAAAAATCTGACCCAGGTCTCAGTTAATTTAG
AAAGTCTATTTTTTCCAAGGTTGAGAACACCCACCCACTCACGACAAGAGC
ATCAGGAGGTCTGACCACATGTGCCCAAGGTGGTAAGAGCACAGCTTGG
TTTTATATATTTTTAGGGAGACGTAAGTCATCAATCAATATATGTAAGATG
TACACTGGTCTGCTAGAAAGGCAGGACAACCTTGAAGCAGGGAGGGGGC
TTCCATGTACAGGTAGGTGAGAGACAAACAGTTGCATTCTTTGAGTTTC
TGATTATCCTTTTCAAAGGAGGCAATCAGATGTGCAATTATCTCAGTGAG
CAGAGGGATGACTTTGAATAGAAAGACAGGCAGGTTTGGCCTAAGAAGTT
CCCAGCTTGACTTTTTCTTTTAGCTTTGTGATTTGGAGGCGCCAAGATTT
ATTTTCTTTTACATTTCCCCCCTTTCTTTTTAAGAATCTTTTAAAGAA
AGCTTTTAAAAGAAAATGAGTCTCTGGTCCCAGGTTTTCATCTGAATTCT
CGAGGGGAGGATGGTTTATCCTAAACGGGTGGTTCTGAATTTTGAGAAAG
TGCATTGTAC

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AAAAGCCATACGAATGAGGAAGAATTAAGGGCCAGAACAAAACAAGAAGA
TGAGGGAAAGTTTGGAACCTCTTAGAGACTGGCTAAATGGTTGTGACCAA
AATGCTGATAGTGATACGGACAATGAAGTCCAGGGTGACAAAGTCTCAGA
TGGAAATGGGGAATTTGTTGGGAACCTGGGCAAAGGTCAACCTTGCTATGA
CTCAGCAAAGAAATTTGGGTGCATTGTGTTTCATGTCCTGGGGATCTGTGGA
AGTTTGAATGTAAGAGTGATGACTTACGGTAGGGTATCTAGTGGAAGAAA
CCTCTAAGCAACAAAGTGTGTTGCTTAGAAATTTCTTTCTTTCTTTTTTT
TTTTTTTTTGAGCTGGAGTTTTGCTGTGTCGCCCAGGCTGGAGCGCAGTG
GCGCAATCTTGGCTCACTTCAAGCTCTGTCTCCTGGGTTCATGCCATTCT
CCTGCCTCAGCCTCCCAAGTAGCTGGGACTACAGGCGCCTGCCACCATAC
CTGGCTAATTTTTTAGTATTTTAGTAGAGACGAGGTTTCACCATGTTAGC
CAAGATGGTCTCAATCTTCTGACCTCGTGATCCACCCGCTTGGCCTCCC
AAAATGCTGGGGTTACAAGCATGAGCCACCCCGCTGGCTGCTTAGAAA
TTTCTAAGCCAGGATATGGCCTGTCTGCTTCTAACAGCCTGTGCTCAGGG
GTAAAGAAATGACTTAAAGTTGGAACCTATGTTTAAAATGGAAGTAGAGT
CTAAAAATTTGGAATAATTTGCAGCCTGGCCTTGTGGCAGAGAAAGAATCC
AAGTAGGCTGCAGAGCAATCATTGCTAGAGAGATTAGCATGACTAAAAGG
GAGCCAAGTCTAATATTCAAGACAATGTTAAAAGGCCTTGAGGGCATT
TCAGAGATCTATGAAGCAGCCCCTCCCATCACAGGTGCAGAGGTTTGGTG
CACTAGGCCCCAGAGGTTTTATGGGCCANNGCCAGGGCCACTGCTATGC
ACAGCTTTGGGACACTGCTGCCCGCATCCAGGCCACTCTGCTCTGGCTCC
ACCCTTGGCTCAAACGGGCCAAGATAGAGCTTGGACCACTGCTCCCGAGG
GCACAAGCCATAAGCCTTGGTGGTTTCCATGTGGTGTAAAGCCTGCAGGT
GCCCAGAATGCAAGATTGAGGGAGCTTGGGCACTTCCACCTAAATTTAG
AGGATGTGTGAGAAACCCTAGGTTCCCAGGCAGAAGCATGATACAGGGGC
AGAGCCCTTGAGAGAACCTCTACTAGGGCAATGCCAAAGGAAAATGTGG
GGTTGGAGTCTCTACACATGGTCCCCACTGGGGCACTACCTGGTGATACT
GTGGGAATGGGGCTGTGCCCTCCAGACCCCAAGATGGTAGATGCACTGG
CAGCTGGCACCCCTGAGCCTGGAAAAGCTGCAGGCACTCAACTCCAACCA
TGAGATCAGCCACATGGGCTACTCCAGGGAAGCCACAGAGGCAGGGCT
GTCTAAGGCCTTGGGAGCCTACCCCTTGAACCAAGCTTGCAGGACATGGAA
TCAAAGATTATGTTGCAGCTTTAAGGCTTAATGTTTTCCCTGTCAATTT
AGGCTTGTGTGGGACCTGTTGCTTTTTTTTTTTTTTTTTTTTTTTTGGT
CACAGGTGTTTGAACCAGAACCAATCCATCTTGAATAGGGGCTGGGTAA
ATAAGGCTGAGACCTACTGAGCTGCATTCCTAGGAGGTAGGAATTCTAA
GTCACAGGAGGAGATAGGAGGTGGGCACAAGATACAGGTAGCGAAGACCT
CGCTGATAAAATAAGTTGCAGTAAAGAAGCCAGCCAAAACCTCACAAAGCC
AAAATGGTGATATGGTTTGGCTCTATGTCCCCACCCAAATCTCATCTCAA
ATTATAATTCCCATATATCCCAACATGTTGAGGGGAGGACCTGGTTGGAGG

TGATTGGATTATGGAGGCAATTTCCCCCATGCTGTTCTGGTGATACTGAG
TGAGTTCTCATAAGATCTAATGGTTTTATAAGTGGTTGGAAGTTCCTCCT
ACACACATGCTCACACTCTCTCCTGCAGCTTTATGAAGAAGGTACTTGCT
TTCTTTCTGCCATGATTGTAAGTTTCCTGAGGCTTCCCAGCTATGCAGA
ACTGTGAGTCAATTAACCCGTTTTCTTTATACATTACCAGTCTTGGGCA
JTCTTTACAGCAGTGTGAGAACTGCTGGCGATGAGAGTGACCTCTGGTT
GTCTCACTGCTCATTATATGCTAATTATAATGTATTAGCATGCCAAAAG
ACACTCCCACCATGACCCCAACAGTCATGCCTGTGCCGGTCTCAGCACCA
TGACAGTTTACAGATGGCATAGCAACGTCTAAAAGGTACCCCATATGGAC
TAACAAGGGGAGGAACCCCTCAGCTCTGGGAAGTGCCTACCTCGTTCCCAG
AAAGCTTGTGAATAATCCACTGCTTGTTTAACATATAATTAAGAAATAAC
TATTAAGCATCCTTAGTTTACAGAGCCCAAGCTGCTGTTCTGCCTATGGAG
TAGCCATTCTTTATTCCGTTACTTTCTTAATAAAATTGCTTTTACTTTAC
TGTATGTAAGTGCCTGGAATTCTTTCTGTACGAGGTCCAGAGCCCTCTC
TTGGGTCTGGATCGGGACCCCTTTCTGGTAACATTTTGACCAATTTCTCC
CTTCTGGAATGGGAATGTTTACACAATGACTGTATCACTTTTGAATCTTG
GAAGTAAATAATTTGTTTTTGACTTTACAGCCTCATAGGTGGAAGGAACT
TGACTTGAATTTAGATGAGACTTTGGACTTTGGGACTTTTGGGTTGGGG
CTGGAATGAGTTAAAAGTTGGGGGGATTATTGGGAAGGCACGATTTTATT
TTGCAATATGAGAAGCACATGAGATTTGGGGGACCAAGGGTGAATAATA
TGGTTTGGATGTTTGCCCCCTCCAAATCTCACATTGAAATGTAATCCCCA
GTGTTGAAGTGAGGCCTGCTGGAAAATGTTTGGATTACAAGGCTGTCGAG
CACATTGGATAAGACGTGTAGGNCCC

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CGCAGCTCGCTGGTTAATTCTGTGGCTCCTGTGACCACTATTATAGCACC
AGGTCTATGACCAGGAGAATTAGACTGGCATTAAATCAGAATAAGAGATT
TTGCACCTGCAATAGACCTTATGACACCTAACCAACCCCATTTTACAA
TTAAACAGGAACAGAGGGAATACTTTATCCAACCTCACACAAGCTGCTTTC
CTCCAGATCCATGCTTTTTTTCGTTTTATTATTTTTTAGAGATGGGGGCT
TCACTATGTTGCCACACTGGACTAAACTCTGGGCCTCAAGTGATTGTC
CTGCCTCAGCCTCCTGAATAGCTGGGACTACAGGGGCATGCCATCACACC
TAGTTTCAATTTCTCTATTTTAAATATACATGGCTTAAACTCCAACCTGGGA
ACCCAAAACATTCAATTTGCTAAGAGTCTGGTGTCTACCACCTGAACCTAG
GCTGGCCACAGGAATTATAAAAGCTGAGAAATCTTTAATAATAGTAACC
AGGCAACACCATTTGAAGGCTCATATGTAAAAATCCATGCCTTCCTTTCTC
CCAATCTCCATTCCCAAACCTTAGCCACTGGCTTCTGGCTGAGGCCTTACG
CATACCTCCCGGGGCTTGACACACCTTCTTCTACAGAAGACACACCTTG
GGCATATCCTACAGAAGACCAGGCTTCTCTCTGGTCTTGGTAGAGGGCT
ACTTTACTGTAAACAGGGCCAGGGTGGAGAATTCTCTCCTGAAGCTCCATC
CCCTCTATAGGAAATGTGTTGACAATATTGAGAAGAGTAGGAGGATCAAG
ACTTCTTTGTTGCTCAAATACCACTGTTCTCTCTTCTACCCCTGCCCTAAC
AGGAGCTTGTACCCCCAAACTCTGAGGTGATTTATGCCTTAATCAAGCAA
ACTTCCCTCTTCAGAAAAGATGGCTCATTTTCCCTCAAAGTTGCCAGGA
GCTGCCAAGTATTCTGCCAATTCACCCTGGAGCACAATCAACAAATTCAG
CCAGAACACAACCTACAGCTACTATTAGAATATTATTATTAATAAATTCC
TCTCCAAATCTAGCCCCCTTGACTTCGGATTTACGATTTCTCCCTTCCTC
CTAGAACTTGATAAGTTTCCCGCGCTTCCCTTTTTCTAAGACTACATGT
TTGTCATCTTATAAAGCAAAGGGGTGAATAAATGAACCAAATCAATAACT
TCTGGAATATCTGCAAACAATAATATCAGCTATGCCATCTTTCACCTA
TTTTAGCCAGTATCGAGTTGAATGAACATAGAAAAATACAAAACCTGAATT
CTTCCCTGTAAATTCCTCGTTTTGACGACGCACTGTAGCCACGTAGCCA
CGCCTACTTAAGACAATTACAAAAGGCGAAGAAGACTGACTCAGGCTTAA
GCTGCCAGCCAGAGAGGGAGTCATTTTATTGGCGTTTGAGTCAGCAAAGG
TATTGTCCTCACATCTCTGGCTATTAAAGTATTTTCTGTTGTTGTTTTTC
TCTTTGGCTGTTTTCTCTCACATTGCCTTCTCTAAAGCTACAGCCTCTCC
TTTCTTTTCTTGTCCCTCCCTGGTTTGGTATGTGACCTAGAATTACAGTC
AGATTTGAGAAAATGATTCTCTCATTTTGTCTGATAAGGACTGATTCGTTT
TACTGAGGGACGGCAGAACTAGTTTCTATGAGGGCATGGGTGAATACAA
CTGAGGCTTCTCATGGGAGGGAATCTCTACTATCCAAAATTATTAGGAGA
AAATTGAAAATTTCCAACCTCTGTCTCTCTTACCTCTGTGTAAGGCAAA

FIG. 3 (26 f 52)

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TACCTTATTCTTGTGGTG'TTTTTGTAACCTCTTCAAACCTTTCATTGATTG
AATGCCTGTTCTGGCAATACATTAGGTTGGGCACATAAGGAATACCAACA
TAAATAAAACATTCTAAAAGAAGTTTACGATCTAATAAAGGAGACAGGTA
CATAGCAAACCTAATTCAAAGGAGCTAGAAGATGGAGAAAATGCTGAATGT
GGACTAAGTCATTCAACAAAGTTTTTCAGGAAGCACAAAGAGGAGGGGCTC
CCCTCACAGATATCTGGATTAGAGGCTGGCTGAGCTGATGGTGGCTGGTG
TCTCTGTTGCAAAAGTCAAGATGGCCAAAGTTCAGACATGTTTGAAGA
CCTGAAGAACTGTTACAGGTAAGGAATAAGATTTATCTCTTGTGATTTAA
TGAGGGTTTCAAGGCTCACCAAAATCCAGCTAGGCATAACAGTGGCCAGC
ATGGGGGCGAGCCGGCAGAGTTGTAAAGATGTGTACTAGTCTCTGAAGTC
AGAGCAGGTTTCAAGAGAAGACCCAGAAAACTAAGCATTTCAGCATGTTAAA
CTGAGATTACATTGGCAGGGAGACCGCCATTTTAGAAAAATTATTTTGA
GGTCTGCTGAGCCCTACATGAATATCAGCATCAACTTAGACACAGCCTCT
GTTGAGATCACATGCCCTGATATAAGAATGGGTTTTACTGGTCCATTCTC
AGGAAAACCTTGATCTCATTTCAGGAACAGGAAATGGCTCCACAGCAAGCTG
GGCATGTGAACCTCACATATGCAGGCAAATCTCACTCAGATGTAGAAGAAA
GGTAAATGAACACAAAGATAAAAATTACGGAACATATTAACTAACATGAT
GTTTCCATTATCTGTAGTAAATACTAACACAACTAGGCTGTCAAAATTT
TGCCTGGATATTTTACTAAGTATAAATTATGAAATCTGTTTTAGTGAATA
CATGAAAGTAATGTGTAACATATAATCTATTTGGTTAAAAATAAAAAGGAA
GTGCTTCAAAACCTTTCTTTTCTCTAAAGGAGCTTAACATTCTTCCCTGA
ACTTCAATTAAAGCTCTTCAATTTGTTAGCCAAGTCCAATTTTACAGAT
AAAGCACAGGTAAAGCTCAAAGCCTGTCTTGATGACTACTAATTCCAGAT
TAGTAAGATATGAATTACTCTACCTATGTGTATGTGTAGAAGTCCTTAAA
TTTCAAAGATGACAGTAATGGCCATGTGTATGTGTGTGACCCACAACTAT
CATGGTCATTAAAGTACATTGGCCAGAGACCACACTGAAATAACAACAAT
TACATTCTCATCATCTTATTTTGACAGTGAAAATGAAGAAGACAGTTCCT
CCATTGATCATCTGTCTCTGAATCAGGTAAGCAAATGACTGTAATTCTCA
TGGGACTGCTATTCTTACACAGTGGTTTCTTCATCCAAAGAGAACAGCAA
TGACTTGAATCTTAAATACTTTTGTGTTTTACCTCACTAGAGGTCCAGAGA
CCTGTCTTTTATTAGTGAAGTGAAGACAGCTGCCTCTCTAAACTAATAGTTG
ATGTGCATTGGCTTCTCCAGAACAGAGCAGAAGTATCCCAAATCCCTGA
GAACTGGAGTCTCCTGGGGCAGGCTTCATCAGGATGTTAGTTATGCCATC
CTGAGAAAGGCCCGCAGGCCGCTTCACCAGGTGTCTGTCTCCTAATGTG
ATGTGTTGTGGTTGTCTTCTCTGACACCAGCATCAGAGGTTAGAGAAAGT
CTCCAAACATGAAGCTGAGAGAGAGGAAGCAAGCCAGTTGAAAGTGAGAA
GTCTACAGCCACTCATCAATCTGTGTTATTGTGTTTGGAGACCACAAATA
GACACTATAAGTACTGCCTAGTATGTCTTCAGTACTGGCTTTAAAGCTG
TCCCCAAAGGAGTATTTCTAAAATATTTTGTAGCATTGTTAAGCAGATTTT
TAACCTCCTGAGAGGGAACCTAATTGGAAAGCTACCACTCACTACAATCAT
TGTTAACCTTATTAGTTTACAACATCTCATTTTTGTAGCATGCAAAATAAATG
AAAAATCTTCTTAAAAAATCATCTTTTTTATCCTGGAAGGAGGAAGGAAG
GTGAGACAAAAGGGAGAGAGGGGAGGGAAGCCTAATGAAACACCAGTTACC
TAAGACCAGAATGGAGATCTTCTCACTACCTCTGTTGAATACAGCACCT
ACTGAAAGAACCTTCATTCCCTGACCATGAACAGCCTCTCAGCTTCTGTT
TTCCTTCCCTCACAGAAATCCTTCTATCATGTAAGNTATGGCCCACTCCAT
GAAGGCTGCATGGATCAATCTGTGTCTCTGAGTATCTCTGAAACCTCTAA
AACATCCAAGCTTACCTTCAAGGAGAGCATGGTGGTAGTAGCAACCAACG
GGAAGGTTCTGAAGAAGAGACGGTTGAGTTTAAGCCAATCCATCACTGAT
GATGACCTGGAGGCCATCGCCAATGACTCAGAGGAAGGTAAGGGGTCAAG
CACAATAATATCTTTCTTTTACAGTTTTAAGCAAGTAGGGACAGTAGAAT
TTAGGGGAAAATTAAACGTGGAGTCAGAATAACAAGAAGACAACCAAGCA
TTAGTCTGGTAACTATACAGAGGAAAATTAATTTTTATCCTTCTCCAGGA
GGGAGAAATGAGCAGTGGCCTGAATCGAGAATACTTGCTCACAGCCATTA
TTTCTTAGCCATATTGTAAAGGTCGTGTGACTTTTAGCCTTTCAGGAGAA
AGCAGTAATAAGACCACTTACGAGCTATGTTCTCTCATACTAACTATGC
CTCCTTGGTCATGTTACATAATCTTTTCGTGATTGAGTTTCTCTACTGT
AAAATGGAGATAATCAGAATCCCCCACTCATTGGATTGTTGTAAAGATTA
AGAGTCTCAGGCTTTACAGACTGAGCTAGCTGGGCCCTCCTGACTGTTAT
AAAGATTAATGAGTCAACATCCCCTAACTTCTGGACTAGAATAATGTCT

FIG. 3 (27 of 52)

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GGTACAAAGTAAGCACC_AATAAATGTTAGCTATTACTATCATTATTAA
ATTATTTTATTTTTTTTTTTTGGAGATGGAGTCTCACTCTGTTGCCCAGGC
TGGAGTGCAGTGGCGCAATCTTGGCTCACTGCAAGCTCTGCCTCCTGGGT
TCACGCCATTTTCTGCCTCAGCCTCCCGAGTAGCTGGGACAACAGGCAT
GTGCCACCATGCCCAGCTAATTTTTTTGTATTTTAGTAGAGATGGGGTT
TCACTGTGTTAGCCAGGATGGTCTCTATTTCTGATCTCATGATCCGCCT
GCCTTGGCCTCCCAAAGTGCTGGGATTACAGGCGTGAGCCACCGCGCCCG
GCTTATTATTATTATTATTACTACTACTACTACCTATATGAATACTACCA
GCAATACTAATTTATTAATGACTGGATTATGTCTAAACCTCACAAGAATC
CTACCTTCTCATTTTACATAAAAGGAACTAAGCTCATTGAGATAGGTAA
ACTGCCCAATGGCATAACATCTGTAAGTGGGAGAGCCTCAAATCTAATTCA
GTTCTACCTGAGTAAAAAATCATGGTTTCTCCTCCATCCCTTTACTGTA
CAAGCCTCCACATGAACATAAAACCAATATTCCTGTTTTTAAGATAATA
CCTAAGCAATAACGCATGTTACCTAGAAGGTTTTAAATGTAACACAAT
ATAAGAAAATAAAAAATCACTCATATCGTCAGTGAGAGTTTACTACTGCCA
GCACTATGGTATGTTTCTTAAATCTTTGCTATACACATACCTACATGT
GAACAAATATGTCTAACATCAAGACCACACTATTTACAACCTTTATATCCA
GCTTTTCTGACTTAGCAATGTATTGATGACATTATGCATGCTTAGACCTC
C

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GTATTCTATTCTCGGTTATAACACAATCACAGTGATTTGTCTATCTTTTC
CAGGATTTGTTAATTTCACTTCTTCAGCTGTTTCCCCCTTGTGGCTGGA
ACTGATTTTCTATCTTCTGGGAGAATCTTCAGCAAGCCAACTCAGGATTT
GTGGGGTGCATTTTGTCAAGTCTAGGACCCAGGCTCTGGGTGACTGATTT
CCTCTAATTACCGAGCAATGTAAAATGAGGAAGTCTGATTGTGTAAAGGT
GTTAAACTTTTGTGTGACGGCAAACTTTAATACCATGAATAGAGATTCC
AGAATTTTCCAACCTCTAACGGGATTCCCTTCACTCCCTGACATTAGAAT
GTAGAAAATCTACCACAAAACATCTGTGAGGCTATCCTACAAGGCCCGT
TTTTCAAATAGGTTTTTACAAGGATTGCTATTTGGGATGATAGTTTCAG
AAAGGCGCTATCAAAGTTAATTGATGATGTGTGCAAGCTGAAAGTTATAT
GTTAGAACTAGCAGTGATTTCAAAAATATCCCTTTTAGGCTTTTTTGCTAA
TATATCTGCTCATTTTCAAAGTTCCCAATATTATAAACTTTTTAAAGCA
GAAAGAAGAACCCTCCATTTCTGCTGGCCCCCTTCCCTGTTCAACTAAAAA
GTATTTTCCCAGGCAATGCTATCCCAGGACTCACACTCCATCCATCCATC
ACCTACCATAAGTTCTTTGAAGGGCTCATTCTGAGCGCTTCTGAGTGCC
TGGGATCTGTTATTTCTCTCCATTTCTGCTGCTGCATGGTAGTCCAAGTC
CTCCTCCCTTTTCCCCTAGGCCATTTGAATCATCTGCTAATTGGTTTTCC
TGATTGCCACGGAACTTCCCTCCATCCCTTCCCTCACATATCAGCCACAGA
AGTATCTCCAAAAGCAAATCTGGTGACATGAAGCCCTTGACAAAACCC
ATTCATTACTGGTTCCACACCTCCTTTGTGGATAAGTTCAAGCTCCTGAG
TGTGGCAAGCAGGGCCCACCTGGAATCCCCTGCCCTCCTCTCCTATCCCA
CGCATCAATCTTTCTGTCTATTTGCAGTTCCTTGAATGTGATATTCTTT
CTAGTCTCTGTGCTTTTGCTAACCTGTTCTTCTGACTGGAACTCCTT
CTCCTCCTTGTAGTTTGGCTAATTTCTAGTCTTTCAAGACTCAGCTCATG
CTTCACCCCTCTATAACAAGTCCTTTCCCAAGCTGGGTGGTGGATGCTC
CTCTGTGCTGTGTGAGTCTTGAACATCCTCAGCAAACCTCAGCTTTGTTT
GCTTGTCTCCCTTGCTGTCAATGCACCTGATTACAGGGCTGGCATATACTG
TTCACCTCCATGACTGGCTCATGGTGGTGCTCCGTGAATATCATCCACCC
AAACGGATGAGAGTACCATGCCATCACTTGTGACTTCCATCTGGAGCTA
ACCTCCCCCGACAGGAAAGCGTTTTCTTAGGAAAGAATATCTTTGGGTTA
AATAGAAGTAGAGACTCACCAGAAGCACTATGTCCAGCTCAGAATGAAC
GCTCAGTAAGCAGCCTTGTCAATGAGGAGGCAGCAGGCCAGCCCCAGAGG
CCTCAAAGTGGGAGAGTAGAGAAGCGCAGTTCCTGCCACAAAGGCACAGT
GGACACCTTGCTCCCCTGGCTGGCTGGAAGCAGATGGTGTCCACCTGCTT
CCATGGGAATTCTGCACCTTTAATAAAGTTTTATGGGACAGGAAGGTGAC
TGGCATTGACATTGTAACGAGGAATGGGTGGTGCCACCTTTGCTGTGTCT
TACCAGAAATACCTGTGGCAGGTAAATTTCTAGAGAGACCTCCCATTTT
TCCCATATAGCAATTTTGAAATGTTTCTGAGGGCTTTCCAAATTCATCT
GGGAACATAGGAGTTCCAGAAAGATGAAATCAAAGGTGATGGTATGCCAA
AGAAAGTAGCTTTTAGAATGACTTACATTAGCCATTATCCATTACGAC

FIG. 3 (28 of 52)

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AAGGAGTGTGCTTGCTGATAGCATGTGTGANGGGACGAGGACTAAATAAT
TTCTGCCTTCAAGAAATTGCAAACTAGTAATGGAGATAAAATCAACAGAG
GAACAATTAGAGTATAAGGTAAAACTAAGGGCCATAAGAGAGGGAGAAGA

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AGTATGGGAGTTT CAGAGG T AGGGGGTAAATGAGGGGAGTAGGTGGGTAGA
AAAGGTTAAAAGTAAATAATGATGGGAAGGAAGACAAAAAGACGACAGGG
GTGCCAAAGGACTCTTAACCTCATCTGAACGGAGTTGCCCTGTTTTGCTC
TCTGATGCTCATGTATCTATCCTTAGAGACAGCTTGGCGGGCAATGTAGA
GCGTAGGGGCTGACATAGGGGGTTGGAGTCCCACCTCCGTGACTTCTAGC
AAATTAGCAAACCTTTGCTGCTGCTAAGCCTATAAGGCGGACAGAAATGCC
ATCTTTAAAGCTTGTATGTAAAGTGCCTAGGACCTCGTAGGCATCAACA
GGAATAATGGATGAAACAAAACAACGGTGCCTATCTTGGAGAAAGTGGCA
TCTGAGCAGGAGTATTTTGAAGGTAGGAAAGGGCTCCAAGCACATCTAA
GAGATTAGGGAACGCAGAAGCCTTAGCCCTGGGTGCAGATTTAACCAATC
AACTTCTAACCACCGCAGGCTGAGAGGTGTGGAGTGAAGCCCCGCCAGA
GGCAGGAGACCCGGGCTTCGGCCAGACCCCGCCTCCTGGTACAGAGGACC
ACGCCCCGCTCTGCCTGGAGCCAAATGTGGATCAAAACAGCGCGCAGCTT
CCCCTGCTGGTGAACCCGAGCAAGGGGGCTCAGTTTCTTTATCCGGA
ACGTGGTGACATGACATCTCTTTGCAAGGCTGCTGCAGGGCTTTCTGGA
AATACGCCCCGTGAGGTATCTGGGCCCTGCGCACAGCCTCCCCCGCCAGGA
CCCAGACGTCTACCTGGGGGTCCCGTCTGCGCTCCCGGGATGGAAAACGC
CCAGGGGAACTTAGGCAGGCGAGCGGACGGGCACCTCCCGCGGGACGAA
CTCACTCGGTGGCCTCTACTTCCCCGGCCGTGTTCCAACGCCTGAGAAT
AACGGGAACAGCGGTCTACTCACCGACAGCGGCAGCAGCGGTAGGCCCG
GGCCCCACCATGACTCTTCAGTGACAGTTTTTCTTCAAACGCCGCSCTG
TAGCCAGGACCGGCGTGCCGCGCGTCCACGCGTCTCATTGGCTCCTGCG
GGTTTGAACTCGCTAGTCGTGACGACGGGAGGGCGGGACAACAGGCAAT
AGGCTCTTTGCGGTTGGCTCTGGCCTTGAGAACCCGACCTTGGGGCCCTT
TGATTGGAAGAAGTGCAGCGCACCTCGGCATTGAGGGCGGCTTCTCTCGG
GGCGCGGCGCCGCCCTCTGAGTGCCTGTGAGTGCCTCCGAGTG
GGCGTGGGACCTCCGTGGGGGCTCAGCCGGGCTGGTGGTGGGGGGCG
GTTACGCTGAATCCAGCTGGGGTTGGCGCGCCGGGAGTCCCTGGGCGGAG
AGACAGGGCGGTCTCTCCAGGATGCTGGGGCCGCTACCTGATTCTGTCCT
TTCAAAGTCTCAGACTCACAGGAGCTGTGAAAAATAATATTATAAAGAG
GACATATGGGTCTTATGCATCTAAAGGCTCCTAGTTCTTAGTACTGCAGG
GTGGCTCGTTTAATTGTGGTAAATATGCATAACATCACATATAACATTT
TAACCATTTTAAAGTGTAAATTTTCAAAAATGTGCAGTTTAGTGGTAT
TAAGTACCCTCACATTGTGGCACAGCCACCCTACTGTCTTTCCAGAAC
TTTTTCATCTTCCCAAATGAAACCCTGTACCCGTCACTAACTCCGCACTC
TCTCCTCCCCAGCCCCAGGCAATCACCATTCTAGTTTCTGTCTCTATGG
ATTTGACAACCTGTAGGTGCCATATAAGTAGAATCATGCAGTATTTGTTCT
GTGACTGGCTTGTTCCTTAGCATAAAGTATTCAAGGTTTATCCATGTG
TAGCATGTGTCAGAAATTTCTTTTCTTTAAGGGGGAATAGCATTTCTGTT
GTGTGGAGATGCCACATTTTGCTTCTTGGTCCATCCCTCTCCGGACACTT
GAGTTGCTTCCACTTTTGGCTATTGTGAATAATAATATGAACATGAATG
CACAAATAACTCTTTGAGACTCTCCTTTTCTTCTTTTGGGTATATACCA
CGAAGTGGTATTGTTGGATCAAACGGCAATCTATTTTTTAATTTTTTGAG
AAACTGCCCTACTCCTCTCACGGTGATCTCTGTTCAAGGTATATTTTCG
ATTTACCTGATCAGCTGACTATAAGGCCATAAGGCTAACGGAGAAACGC
AGGCCTAGTTTCTCCTAGTTACTAGGAGATCGCAGGCCTCGTTGTCTCTGA
ATCCCTAGACACACTTCTATCCCTTGTTTAATCCTAAATTTTTTTCT
TTTGAAGTTTGTCTGTTTCTATCTATTCTCCAGTTTCTTAAAGAGGTCTG
GAAAATGCTTTTGGCTCCTTGTGTATGAAGGTTCTCTTCCATGGATGCT
GGAGAAGTCGTGTGTGGAGGGGAGTCATATCTGGGCACCTGTTGGCCAG
GTTGAGCTTACCAGTTGGGTACTCAGCAGGGCATGAAGCCACTGCAGCAG
CCCTTCTCTTTAGCCGTAAATAGGGAGTTTGAAGAGAGCCAGGGTTTCT
GGATTTATGCATTTTGTATTTTCAATAGTGTATTAAATGTTTAAATAG
GAAACTGATCATTATTTTGTAAATGACTGAGAAAGGGACTCCTTCACC
AACAGTTTCAGAAAAGTGAAGGCGGTTTTGTTTTGGTCTTTGTAGAATCT
AGGTGGTTGAATGCATGTGAGTTGTAGAAGTCACCTTGCTGATATCCCA
CGCAGTGTGGAGTATCCACAGACCCCATGTAGGTACTGCACCTTTGCA
GGTATACTGCTGGTGTGGTGGAGTGCCTTACCTGTCTGTTATTGGAGA
CCCCTGCTTATTAGGAACTTAAATGAAGTCAATGAGCTTCTTGTCTT
ACTGGTCTAGTCTTTTGGAGCAACATAGGCCAGTTCTGCCTCGTTTTTT

FIG. 3 (30 of 52)

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TCCATCCTTTGGGTATTTGACGGTCTATTTTGTAGGACACAAAATGTGGG
AAAATAGCTAGGCAGGTTTAAAAATTCTCAACTCTACCAAGCATGGTGGC
TTATGTCTGTAATCAATCCCAGCACTTTGTGAAGCTGAGGCAAGAGGATT
GCTTGAGCCTAGGAGTTTGAGACCAGACTGGGCAACATAGCAAGACCTCG
TTTCTTAAAAAATAAATAAATTACAAAATTAACCAGGCATGGTGGCA
CACACCTGTAGTCCCTTCTACTCAGGAGGCTGAGGTGGGAGGATCACTTG
AGCCCAAAGTTGAAGGATGCAGTGCAGTGTGGTCATGCCACCGCACTCC
AGCATGGGAGGCAGAGCAAGACCCCTGTCTCCAAATAAATACATAAATTAA
ATTCTTAACCTCATTCAATCAAAAGTATCCACTGTAGCTTTCCATCATCCTGG
TGTTGTTTTTTTTTAGAAGGATCTGGCTCCATTGCCCGGCTAGAGTGCAGT
GGCATGATCTCAGCTCACTGCAGCCCCACCTCTCTGGCTTAAGCGATCA
CCCACCTCAGTCACCCATCTGGGTAATTTTTGTATTTTTTGTAGAGATGG
GGTTTTGCCATGTTGCCCCAGGTTGGTCTTGAACCTCTGGCTCAAGCGAT
CCATCTGCCTCCATCTCCTAAAGTGTGGGATTACAGGTGTGAGCCACCA
CACCAGGACAATCCTGGTGGCTTTTAACGGTTTTCCATTGCTCTCAGGCT
AATGACCTATAAGCCCCCTGCGGGCTTGGCCTTTTACTCCCTEAGCATTAG
CCACCTCCCTTAGCCTTAGCCCACTACTCTCCCTTGCTCAGTGTTAT
CCAGACACTTTGTTTTTCTTTCCATACTCCTCTCTGTCTGGGAATCCA
ACCTTTCTTTCTCATTCTCTAGTTGATTATTATTATTTTTACTCTAGCA
GCCTTATTGAGATATTTACATACCGTACGATTCTCCCACTTACAGTGTAC
AATTCAATTTTCTAACATTTTCATCACCCCTTAAAGAAACCTATACTCA
TTAGCAGTCACTCCCATCTCTCCCTCCTCTCAGCCCTAGAAAACCATGA
ATCTACTATCCATCTCTATAGATTTGCCTTCTGGACATTTCATATGTATG
AAATTATGCAATTTGTGGTCTCTGATGGGCTTCTTTTGTTACCAAATAT
CATGGGTTTGATCTAGGTCTGCTGCTCGCTGCACAGAAAGCCAGCCACT
GAGATGACAAGTATTGCCAAGGAAGAAGGCTTTAGTCAAGGTGCTGCAGCT
GAGGAGATGGGGGCTCAATCTCAAATCCATCTCGCTGACCTAAAACAGG
GGTTTGGATAGCAGGAAGAAATGTAACAATGCGTAAGAAAACAGGAACC
AGGGAGGGGCAAGGAAGCAATCCTGATGAATGAGTGGTCCAAAGTCTCAT
TGCCTGGATGTGGTGATCTGGCGAGTTTCAGTTCTTTGATACTTTTTTTG
AGAGGCCTGAAGTCTTTTCCCCAGGAAGGAACCTCAAACAAAACAAATACA
AGCTTCCAGCTTTAAGACCAGAAGCGTCAATTTCTATGTTTATCCGAAAG
AACAGTCTATGGGACTATTGGTTAAGTTTCACTTTCACTTAGTATGCTGT
TTTCAAGGTTTATCCACATAGCATGTGTGAGTACTTCATTCTTTTATGAC
TGGGTATTCTATTGTGCGGATATACAATATTTTATTTGCCATTATCAGT
TGATGGACATCTAGGTTCTTTCCACTTTTGGCTATTATGAATAATGCTG
TTATGAACTTTTCATGTATAAGTTTTTGTGTAGACATATGTTTTCAACACT
CATGGGTATATACCTAATGAGAGGAATTACTGTGTATACGATAATTCTA
TCTTTAACCATTTGAGGAAGTCCAGACTGTTTTCCAAAGCAGCTGCAGC
ATTTTACATTTCTACAGCAGTGTATGAAAGTTCCAGTTTCTTTACATCC
TCAACAACACTTGTATTGTCCATCTTTTAAATTACAACCATCCTAGTGG
TTGTGAAATGGTATCACATTGTGGTTTTTATTTGTATTTCTTTGATGACT
AATGATGTTAAGCATCTTTTTATGTGTTTACTGGCCATTTGTATATCTCT
ATTCAAGTCTTTTGCCAATTTTTAAATTGGGTGAGTTGTCTTCTCTCTTT
TTTTTTGAGATGGAGCCTCACTCTGTTTCCCAGCTGGAATACAGTGGTGT
GATCTCAGCTCACTGCAACTTCCACCTCCTGTGTTCAAGTGATTCTGGTG
CCTCAGCCTCCCAAGTAGCTGGGATTACACGCACCTGCCACCATTTCCAG
CTAATTTTTTTCTTTGTATTTTGTAGTAGAGACGGGGTTTACCATGTTGG
CCAGGCTAGTCTCTTTGTGACTCTTAACCATCCTTCAGTCTCAGACAAA
ACATCCCTTTCTCAAGGATTGTGATTAGCTTGATTATTTGCTTATCTTTT
TCCCTGCTAGTCTGTAACTGAGGGTAGGCCACTATATTTCATTGTTCTTG
GCACCAATAGAACTAAATTAATGTCTTTTGAATGAATAGGGCTTTCTC
CTTTTAAAGATCCCTTCAATACAGTAACCACACTATATATAAGTAGCCAC
AAGCCCATTCATAATACTACTAGTNCTTGGCCCAAACC

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GGCTCAGCGTTACTATACTGGTCTCAAACCTCCTGGGCTCAAGCGATCTGC
CCCCCTCGGCTTCCCAAAGTGTTGGGATTATAGGCGTGAGCCACGGTGCC
TGGCCTCAAATAACTATTTAAGTGAACAAACTAGTATGGCACTAATGA
AAAATGTATAAATCCATAATCGCAGAGGGATTCAACTTACTTCTTTTGA
TTATGTAAAGGTCAAACAGACAAAAGACAATGACAAAACCTAATGCAATG

AACACTTTTGATTTAATGAACATATATTGGATATGTACCCAAGAATTAGA
GAATACATACTAGTTTTGAGTTTATGCAGAACATTTACAAAAATTTAGTG
GAAGCCTAAATTATAAAAAGTTGCTGTCACGTAGAATAACACACAAACCC
CTGAGTCCGGAATTCAAAGCCCTCCACACTCTCCTCTACCTTTGCATCTT
TATCCTCCACCACACTGCAGTGCATACTCTGGGCTACTACTCACTGTTCT
TGATTCAAATTCATGTCTGTGCTCAGCTCAAATCATTCTCTCTGCCTGGAA
TAAGTACTTTCATACATATTCTGCTATTGAATTTCTTGTCTTAGCACCCCAT
CTACTCCAAGACGATGTCCAGTTGGGGTTACTCCCTGTCCCATTTTCTTT
GATTACACTTTTTTTTTTCTACTTCCATTATATTATTGATCACATCTGTGC
CACAGTTTTTTGACTTTGTGTCTGCTTTTACTCTTTTCTAGACCCTGATAG
CTCCTGAAGGGTTGGGTCATTTCTTTTTTATTTGCTCATTCCTCATGGCA
CAGTGAGTGCTTAATAAATGGCTATTGACTGAAATTAACTGTATCTAAA
TGGACATATTCCACTTCTGGGCCATTCTTTCTTTCTATTGGAACCA
GGAGATGGGGAACCATAACAAAGGTAAGGTTGTGCCATGTGAAAGAACAT
GGAACCTTCCCCTGAGGGCCAAAAAGAGCAGGGAAAGGTGCAAAGACAA
AATCTTCCATTTTTTAAACAATGTAAGAATGTGGTCCACCTCATGCTCAGG
TGGGACTTTTATCATGACGTTATTTTTTGGGGACTTATAGCTGCATCATTTA
CCCCATATACATTTACCTTTAGTGTAGGGAACAGGACAGGAATTTTGT
TGATGCAGACTCTTGCTAATGAGGCTAACACTTGGAGAATTTTTATCATG
CATTCAAGAAGCTTGTTTTACATTTCTTCATTAATACTTTAGTTGGTGGT
TTAGCTTTAGTTGTAGGCTTATCAGATATTTGGAGATATCTTCATAAACC
ATGGCTTTGGTTTTAGAAGAGTTATTCTGAAGCTACTATTTCTGGCAATA
ATCAAACAGCATGGCCATTTGTTTTGTAAGGCCTTCTCTAGAAATATGACG
GTAAATCTACGTGTGGAAAAATGCTTATTCTTCTGTCTCTATAAATGT
GAATCTAGTTTGTCTTCAAATGAAATCAAGTGATTAAATGTAGTTTTTC
TAAGAAGATAAATGGAGCAAAGCACTCTGTGTTTCACAGTGTTGGAAATC
ACTCATCCCTCATAAACTGTCCCACTGATCCTGACTCACATGAATGAA
TTAAATAAAGAGTTAATAACATCAATTTACATTTTTAAAGACACTTTCCC
ATGTTTTAGACTATTGGTTGGAAAAGCTGGTAGGTGTACAATTTGTGGAG
AGTTGGCTGTTTTTGTCTGTCTGTTGTTGACGTATTTCAAAGCCATATCT
AATTTTGTGTCAGAATGGTCTGAATTCTACAAAAATGTTGAGTTGTGTAG
TGTGGAGAAGTACGGAGCCATTTACTGAAAGGCTGGGGGGAAATGACGAG
ACCCTGAGATAAGGCAGTAGTGGTGCGAACAGAGTGGAAGGGAGGTAGTT
GAGATATGTTTCAAGTAGAATCAGAATGGACATAGTGAACAACCTGGATGC
AGGTGGGGGCTGAGGAAGCAAAGTTGAGGATAATTCTGAGACTTCTAGGT
TGATCCACTGAAGTTACATTATTCAACACCACAAGGAACTAGGGGAATG
AGAAGGCATACTGGTTTGCTTTGGAGTGGAAGGGCAGTGATGTAAGAGGA
GTTAATGAGTTAAAGTTTGGATATGCCTGAACCTCAATTTGATATGTGCA
TCTGATATACCTTTGGGGTGACCTCCAGGCAATGTTGAACATGTGTAT
TTCTTAGTAAGTATAGGCATCACAGACTCACATCAGTAAGGAAGCAACA
GCAAACCTTGATTGGACGATATACCTGGAACCTCAGTACCCTATGACTGGAG
CAAGTCTCTGTGCTGAGTAAATGAGGATAAGAAGAATCTTGACCTTGTGGAA
TATGTTGTTAGGAATATATGTGATGAACAACATAGGATACTTCTACAGG
GCTCCACATGTAGTAAGGGCTTTATAAATGCTTGATAAATATTATTGTTG
TAATTTATTTCAAAGTAAGATGCCACTGGAGGAATCTTTGGAACCCAAA
TTAATAACAAATAGGACTGGATGCAATGGCTCACACCTGTAATCCCAGCA
CTTTGGAAGGCCAAGGCAGGAGGATCTCTTGAGCCAGAAATTCAAGACC
AGCCTGGGTGACACAGGGAGACCTTGATCTATGAAGAATTAAAAAAAT
TAACCAGATGTGGTGGTGACGCTTATAGTCCCTGCTGCTTGAGAGGCTG
AGGTGGGAGGATTGCTTGAGCCCATGAGGTTGAGGCTGCAGTGAGCCATA
ATTGTGCCACCACACTCCAGACTGGGTGACAGAGTGAGACCCTATCTCAA
ATAAATAAATAAATAAATAAATAAATAAAGTACAAACCAGCAAACACTAAT
CCTTTCTAGAGATTATTGAACTCTGGAGGGCAGATCTGAATGGAGCCAGC
AGAGGGACCTATGGAGATCAGCCTGGCCCTGGACAGCACCAGGCAATGGG
GTTGCTAGAGAGGTAATGGGGTTGAACAGGGTTAAGCCATGAGGTCTCA
AGAATCCGTGAAGACTCAGACTAATTTTTTTTTTTTTGTCATGAGGATTAG
GTGTTCTTAGGAATTTCAATGAGAGCAGGGTTAATGAAGGAATGCAGGGT
AGGAGAGCTGAGGGAAGGCATCTGAGAGAGCCTGGCTTATGAATGGCTGC
GTCAGTATGGCTCACCTGCTTTCTTGATCTACTTAGCAGATGATCCCA
CCCCAGGCCTCCAGGGCCAAGGTCATTTCCACATAGTCATGGGCCCTTGA

GGGCCTGGAGCAGTGTAAAGAGACAGAGTCTTAAGAAATTGCATTAAC.
GTCATGGTGCTTGGCAAGTGTCTGTCATCCTATGCCAAGCCTGATCTGAAG
GGGTGCATGCTCATAGGTAGCTGCTGCCCCAAGATTACAGCAGCTTCTTCA
ATCCAGATCCATGCTCTCCTATATTCAATTTTCCAGGGGTTCTGTCTCT
TCGACAGTGTAGATGCAGAATGACTTATTGAGTTATTCTCCTGATAGT
TGCCAACTTTTCCAAATGACAATGGGGCATGGAGCTTGAGAGTGGAAATG
AGGCCCTAGGGATAGCGTGCTTAGGAAAACACTCCCAGCCTGATGTAATT
CTGGGGGTACAATGGCATTTCATCATCAAGACTGATGTAAAGGGTGACT
AGCAGTGAAGTTGGGGGTGACTCGCACTGGGGCTAGGTTTCTGATTCTGCC
TAATCCAGACAGAGCAGAAGCACTAGTGGGCTGGTAGAGGGCCTCCAGGG
CCTCACTTAATGTCTTGGAAAAACAGCTCCAGATTGTTGGTTTCACGTTCT
GAGGACAAAGCTTGGGTACTACAGGATAGAGAGAGTGGTGGGAGATGCCGT
GGCCTGCCCTGCTGATGCCCTGCCCTGCCATTCTGCGTGTGATGTCTCTG
GGGCATCTTGCCTTCCCTGCCAGACCTGTAGTTTCAGCTGAGGGCATGTG
GAGGCCAAATGGCTTCTTAGAGTGTACTTTCTTGAACAGCTCTGCTGG
GAGAACTGGAGGAGCTAGCTAGTCACGGTAACTGCAGCAGTCAAAGGATC
GTCCCGGTGGAGGTGGGGTGGAAAGGTAGAGAAAGAGAACATATAGCGTT
TTCCTTGGAGATGTGTGGGCATGTCTATAGAGGAAATACCCAATTCCTGAG
CCTTGAGCCCTCCAGGAAACCTTGAATATTAGGTTAGTCATCCCCAAGG
AAGTCTAAGAATTCTGGTCTCACCCATCTCCTTTAATTCACCAATGATC
CTACATGATATTAAGGAACACGGGCCAGTAACCCCTCCAAGCAATGGATGT
GGTGGTGAAGTTTGACCTCATGATGGAGCGGAGGTTGGTTTGAAACCTAA
GAATTTAATTTATTGTTTCAAACCTGTTCTCCACTCAGCGTTATTAAAGCA
TACATAATTGACACATAAAAATTGTATATGTCTACGGTGTACAATGTGAT
GTTTCGATCTATGTATACATTGTGAAATGATTACAACAAGCTAAATAACA
TACCCATTTCATCGTGTTCAAAGGAATTAACTCAAGCACAAAAGAGAGG
TGCTGTTGAAGAGTAGGGCTGCTCTATCTAAGTAGTATGTCTGGGGTTGT
CCTGGATCAGGGTCTTTTGTGCTAGTAATAAACCAGCCCTTCTGGGGCT
GCTCCACTTTCCCCACATTTTCTTCTGGAGCCTCCCTAAGAATTAGGACA
TGGCCACTTTCTCTGCATAGGCTTCTACTTCAACAAGGACAGGGCTTGT
GCTGCCCCATGCCACTTGAGTGTCCCTACAGCACAGAGCTGAGTGCACAC
TGGCTGAGTGAGGAAATCCCCCAGATTAATCTTGGTTCTAAGCATCATGG
CTGTATTTCACACGTATATGAATTACAAATTACAGCATAGTCGAATAAGG
ATTTTGTGCTACAACCTGGAATCCCAGATTATGCAAATTGGATAGTATAA
TATTGAAATTCCTAGGACTTTTTATTAGTTTTTAAAAAATTATACAAGCTT
AGAGTAAGAAATTAAACAGTGCAAAAAGAATTCAGTGTGAAAAGTAAATG
CTCTGTCTCTGCTGAGAGACAGATATTGCAGCCCAGATACTACTGGGGTC
AATAGTTTCTTTAAGCATGCCATTTTGATGGTTTATGGGACTTACAGCT
CAAGAAGCTTGACACTAGGGTTGATCTCAGAAAATCATTGTTGCAGGTAT
TAGATATGACCGTCTCATAAAGATACACACAGACACAGCGATTGGAGA
TATTCAGTGGGGCTTATGGGCTGCTTGTCTTTCTGCTCTGTGCCTAAGT
TGGGCTCAGAGTAGCCTGGCATCGGCTGTGGGGAGAATGCTGGCATGGGG
TTAGCAGGAGCCCACTTAACATGTCTAAGCCACCTGGAAGAGTCCTTCA
AGGAGACCAGACTCCAGAGGCCCTAAGGAAGGAAGGACTTTTGCCCGTTT
TTAGGTATTCTAGTCCCAGAGTTTAGGGAGGAATGGTTTGGCTTTGGGTC
GTGTGCCCCCTTACCAGAGTGGGATGGGATGTGCCCATGAGCTGTTGAGCT
GGCTCTTGGAGAAGACAGCAAAAGCGGGAATAAGAGGTCAGGAAGCTGTG
TGGTTGTAGGAAATCCCAGCAGAGGGCCTGGGGGTCAAAGTGGTCATGG
TAGTGACGGTGGAGGCTGAGGTGGTAGAAAATCAGAGGACAAACCCCATG
GGCTGCTGGTGATCTGACCGAGCTCCTATGCTCTCCTGGTTCAATTTAGG
CTCTGTAGCAGCAGATGATTGGCTGGTGTGAGAGCAGTGCACCTGCCATA
TCAGGCAATCCAAGACAAGTCCAAGCTACGCTGGGAGGAAACCTGAAGGC
AGCAGCAGGTAGACTGGCTGAAGACAGACAGGCAGGCAACTTGTCAATCA
GATTTGTGTTTTTAAGGACTTTTAAGTGGGGAGCCCTCCGGGACAGATCA
GATGAGAGTGAAATGTGCTCCGCCCTTAGCC

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GGCCGTTCCGAATTCGTGTAAGAGGGAGAGTGGTTTTATTTATTTTAAAC
ATAGTCAAGCTGCTAAAGTATATGATATGTATAGATAGAGTATAATTAA
TACTTTCAACTACAGACAAAATCAGGAGAATGGAATTAAAAACAATTTA
CAAATGGGTAATGGCAGCATTGGGTTGCGCCCAACCCAGAGAAGGCAGAC

FIG. 3 (33 of 52)

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ACCAAGATTCTAAGATCAACGTGGCCAGCACTTCAGACTTCAAATAGAA
TTCGTGATTATGCATTATTTTTCTCGGAAAGTTTTCACTTCACTATATGC
TACTTGACACTTGCTTTTCCTAAGACATCCCTCTATTTTTGAGATGACTAA
CTCAGCAATTCATTTCTCTCACGCATAAGCTGTCACTCAACCCAAACCCA
CCAAGCCTGCATTCTACCCCTCAATAAGGTCTTGGTGTGTAAACTGACCCA
CTTCACCTAGTTCCCTTAGCCCTCTCTTGACCAGACATGACTCTTTCATAA
GCTAGACCTATAAAGTCAGGGCTCTTAAGTAGCTGATCTCTGATAGTGCC
AAGTGTCCCCCACTGTTTACATTTTCCACTCCAGCTTCTAACAGGTGATA
GACTGCTTTTTGGGGGTAGGGGACCCAAACATATAGACCTCATGTTTGG
ATGTAGACACTCCAGTTTTCTTTAAATTACAACATACATATTAATAATGACT
TCCAAGTGTACATTTTCACTCCAGATCTCTCCCTGGATCCCCAACTTTGT
AAAACCCACCGCTAGTTGATATCTTTTGATGTCTGACAGGCATTTCAA
TTAATACTGTCAAAACAAAGTTATTGATTTTCATCTCTGCATCTGTTA
CAAATTTTTCTTACTTTTGGTAAATAGCACCCAGGCTGTGTCACTGCCAA
GAACCTTCCACAGCTCTTGGAAATAAATTCAAATATTTTCCAAGGCAGA
AAGGCACAGTGTAATCTGGCTCCTGCCTACCTCTCCAACCTCGTATCACA
CTAGTCTCCCTGTCACTCACCCCTCCAGGAGCTCAGGTATCCTTAAAGT
TTCTTTTCTTTTTTTTTTTTTTTTTTTTTTTTTTGAACAGTTTTGCTCTGTT
GCCCAGGCTGGAGTGAAGTGGCATGATCTCAGGTCAGTCAACCTCCGCC
TCCTGGGTTCAAGTGATTCTTGTGCCTCAGCCTCCCAAGTAGCTGCAATT
ACAGGCGCGTGCCACCACACCCGGCTAATTTTTGTATTTTTAGTAGAGAT
GGGGTTTTCAATGTTGGCTAAACCGGTCTCAAACCTCTGACCTCAAGTG
ATCTGACCACTTCAGCCTCCCAAGGTGCTGGGATTACAGGCGTGAACCAT
TGTACCCTGCCTCCTTGAAGTTTCTTGATCCAGACTCATTCCTGCCTTAA
GGTCTTGCATCTTCAGTCCCTCCCTCAAATGACACCTCCATGAAGACGCA
ATTACCTGTAAATTACCGTGTCTTATTTAGTCAATGTGTTGGTTTTCTGTC
TCCTCCACTACAGTGTAAGCTCTATGAAGGCAGAAACCTTGGCAGTCCAG
TTCCCAGCACAGTGCCCTAGCACACATAGGTATTTAATAACACACAGTAAA
ATTCACCTTTTAGTGTGCAATTCTGAGTTTTGACAAATGCATCAAGTCAT
TTAAGTCTGACTATTATCAAGCTATAAGATGGTTGCAACACTATCACTAA
TTCCCTCATGCTCCTTGGTAGTCAGTCTCACCCCTAACGCCCCCTCTG
GCAATCACTGATCCGTTTTTTGTCTTTATAGTTTTGGTTTTTCCAGAATG
CCAATAACTAAGTTTTGAATGAATGAATGCTATTAACCTCTCATTTCTGAC
TCCAGAGCAACATCCATGCAATATTTATTATTTAGCCCCAAATACTGCC
CCCTCAGCTTCACTCCAACCACCTACTTGATGATACAAGGTGAGACATTT
GGCATGTGCTTCCCTCCATGTTTCTTAGCATTTTCCCTATCTCCTTAGCCTT
CCTTCTAATCATAAACGAAGAGTGAACCTTCCCTTCTAAAGGCAACTTA
CTCCTAGGACCTCGATGCCATAATTTTGTCTCTAGTACTTTCTATATA
TACACCAAACAATTAGCTCCAGAAAGGTAAAGACTCACTGTGTGCTCATC
ACTGTGTCTCTAGCGCTGGCACACTGCAGGTGCTGAAGAAACACCTAC
AGAATGAGTGAATGAATCTCTCCCTCTCTAGACTCCTTCTCTTTTGTAA
CAAACATGTTCAACCTGCAACACAGTCTTATGACCAATCCTCTGTTGTCT
GACCTAGGCTGAGCTCCAGGGCTGGGACCCTGACTTCCTTATTCACCACC
TCAAGGTCTCTGCACTCACTTCTCTTTCTGCTCAGGATTGTTTTCTTCT
TGTCACCAGTCTTTTCTCAGACTTAGGTCTCAGCTCAGACATTGCTGTTG
AAAGTACTCTACTGATCCTTTTATCTAAAGCAGCCATTCCAGCCCTACT
CTCTTGATCATAGCACCCCTGAATTAAGTTGTTTACTTACTGTCTCTTCTCAG
GAGGGCAAGGAGCTTGGTGGTGGTGTTCAGGGCTGTACCAAGCTGTACCT
TGCTTCACCCTGCTACACTTTTTAGCAACCATCTAATTTTACATGCTCCC
TTCACTCGTCAGAAATTTCTTATTTTCTACTTCAAGCAGGTATACATAT
GTGCTTCTCCTGGGAGGCTCACCCACTTCATGAGACTACATTTGGTCTG
GGTAGAAAGGTACAAAATCCACTGGCTCAGTTTTAATCAATGTATGTTA
ATATTAACCAACCTGAGATCTTGATTTCCACGCCTGGCTAATTTTGTATT
TTTAGTAAAAACAGGGTTTCTCCATGTTGGTCAGGCTGGTCTCGAACTCC
CGACCTCAGGTGATCCGCTCACCTCGGCCTCCCAAAGTGCTGGGACTACA
GGCATGAGCCAGCGTGCCCGCCTAAGATCTTGATTTCTACCATCTGAAC
TCTGTATTTGAATGACTGCTCCTGCTTGAGCTTACTGGCCAAACTTGG
CCCACTCAGACTCACGGAAGTTTCTGGTTCTTCCCTGGTAACCTTTTCTGA
ACTTAACCACTGGTTTGTCTGACAAGAGATTACCATCTTCTCACTTCTTA
GCTATGTGAACCTCACTTATCTGCTCTATTGCTGTTCACTTAGCACGGCA

FIG. 3 (34 of 52)

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CTTATTGAACGAGTGTCTACATCTGCACCCCTACTTCTTACTCATCCAT
TCTGTTTCAATTTCTTAAAAAGAAAAAAAAAAGCTATTGTAAACATACG
ATTACAGAAAATGATTATAACATGTGTATGTACCACCTAGCCCTGTCAA
GTCTTAATATTTGTTATATTTGCTTCAAATCTTTTTTTCAGACTGTAGTTA
AAAAATTACTTAGGAGCCATTATTTATGGCCTATTTCTTGACCTAGTCTTC
TTGATGGTCAATTTGCCTAATCATCTTAAGTTGCAAAAGCTTAGAATTAA
AGCAAAGTACCTTCGATCCTCTGCTGTTGCCTTCTTTTTAATATTTGGGT
TTGTTTGGGTCCCATTACGGTTGTGACATCAGCTTGAGTTTGGGAGCT
GTCTTGTTCAGAAAATGGTTCTGGGGAACAGCCTTTTTCAACTTGGAGTC
CAAAGTCTGTGCTTTTTTGCTGAAAGCCATTATTGTTATGTTTATTACCAC
TGGTTCATTGGTCTTATGCTAGGGGTGCTTGAATGGCTGAATTAAAT
CTGCCAACTGTCAAATTAGGCCTCTGGCTTACGGCTTTTGACTTTTGCG
TACACATGATGTCTGAGGTATACAACTTGGCTGGACTTCTGATCTTGCT
TGATGTTTGGATGTCTGTTGTTATATTCACCTGAAGCAAAGTGGGTAT
GTTCTGGGTTTGGTGTGCTTCACTCTCTGTTCAAGTACAGGGTATGACCG
TATCTTAGTTTCATTTGGTCTTTTCAATTTGACTCCTATTAACCTTTATAT
CTTTGATGTTCTTGACTACTGGTTTCTTTGATGACTGAACTTTACTAAGG
GTCCGAATAAAGAGGAGAGGGAACCGTCTTGGGGTTTTACTCCTGGTCT
TGCAAGATCTGCTCCTCTAGAGAGTTGCTGTGATTTTACTGGGAAAGTCC
TGCTTTGTGTTTCTCCAACAAATTGTTTATTAACCTATCTTTTCAAGACA
GCACTATTAAGTGAATTTTGGCCAAGGCTTGTGTTAGGAACTAACTGTT
CTTGGTTTTGATTATAAGAGTCAGTCTTTGGCTTACTTCTGGTATATAATT
TAGGATCTGGCTTCTCTCAGGTTCTGTTAAGATATCTAGCAAGTTCTCT
TTGTTTGTGTTTCTTTAGAAAGTTATCCAAGATTCGTTTTCAACATGGAT
ATTATTCATAAAGTCTATACATTTTACCATTTCTTGATCTGTTAACTGCT
GCTTTGTAGTTTCAATTGCTCTATATTAAGTGACCCACAGGTTTTCTT
GACAGTCTCTGTGGTGGACTATCTAGCTTCACTGTTGAAAACCTCTT
GCTGAAAAGCTTAGACTATGGGTTAGAAGAAACACATTTTGAAGTCCGCC
TTTTGCCCAGAAGTTTTGGTGGCTCTAAGTTTCACTTCTGGGACCTTGCA
GTATTAGGTGGTCTGGGCTGGAGTTTAAATGCTGATGGACCTTTTAGGTTT
GACAGGCAAAACAACATGGTTGGTAACATCATTTTTGGGTCTAATAGTCT
GAAAAACAAGAAAAATACATATTAATAAATCCTTAACATATCTTATTGT
TTTTAAATAATAACTGTGTTTAAACACATGCTAAAAAATAATCATTTTT
AGAATTTTCACTAAGAAAGTTGAATCCTCAGAAAGTAAAGAAAGACTCAC
TAATAGGTAGTTTTTGTGTTTTTTTTTTTTTTTTTTTTTTTGGAGACAGGATC
TTGCTCTGTCAACCCAGTCTGGTGTGCAGTGATGCAATCTTGGCTCATTGC
AACCTCTGCCTCCTGGGTGAAGCAATTCTCCACCCCAACCTCGCAAGT
GGCTGGACTACAGGCGCATGTCACTACACCTGGCTACTTTTTTTGTATTTT
TAGTAAAGTTGGGGTTTACCATATTGGCCAGGTTGGTCTTGAAATCCTG
ACCTCCAGTGATCCACGCACCTTGGCCTCCCAAAGTGTGGGATAACAGG
TATGAGCCACCACACCTGTCCTAACAGGTAGTTTTTACAACCTTGAGTTCC
TATCAGAAGTATATTAGAATCTTTTAGCTTGACAGAATTAAGCAGAGATG
CAGTGAATATACAAAACCTTGCTCTTTCAAAAATGAATTTGCCTCAAACAG
TAGTTGTTGAATGCCTATTATATCCTAAGTGCCCTCCAAAGAACCCTGAA
AAAATACATACATAATGAACCTTATGTTAGGGTACCTCCCAACAAATCTCT
CCTAGTACTTTGTATAGCCACACTATATGTTTTTAAACCACTGCCTTTG
TAAACATCACAGTATCACTCAAGAACCTCTGTCTCATCCCTGGAGATCAG
TGACAAGGAGATAGGTGGCAGATGATGTGAGGCCTGAGATATGCTGCCAC
AGCTCTCAATAAACATGTAACATCTTAATAGTCATATTTGTAAATCAGC
CAGGACAGGGTTTTAAGGTTAGAGTCTATGTTAATAATAACAAATGTTT
AGTCATGTGATTTAAGTTTGGATAAGAAAGGTAGGACTCGATTACAGAGA
ATTTTGAAAACCTAGGGAAGGGAGTTTGAATTCATATGGTAAGTAATTGG
GCAAGCCACTATGAATTCCTGAGCATCTCTCATGAAAGCAATTACTCAGA
AAGGAGAATTTACAGAGATTTATGGAATATGTTTCCAGGGTAAGATATG
GGAATGCTAGAGTTACCACTCTATTTTTGATTGACAAATATTGTGAAGA
ATCACTACATAAACTTGGCGAGTATGTAAAGGATTCTAACCAGAACCAT
TTGGCATTGAGGGCAAAGAAATGTCTACTCTGGATGATAGCGGTGTGTGT
GGTGTACTAGGAGTGAAACAGCGGAGTTGGGAGTGGGAGGCAGAGAGAT
GGATGGTATACCCCAATGGCTATATCTGGATTAATCTTTGAGCACCAC
ATTTATATACACCTCGGATCTCTCCATCATTGCTTACTGAAGAGGTGGAG

FIG. 3 (35 of 52)

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GGACGTTGGCATGAAAGCCTCCAAATGTGTTTTTTTAGTTGCTTTCTTA
ATATTA AAAACGAATTGATATAATCCACAAACCATAAAATTACCATTTT
AGTAAGTGCACACTTCTGTGGATTTTAGTATAGCCACACTATTATACAGC
AATCACCACCTGTCTAATCCAGAACATATTCATCACCCCTAGAAAGAGAC
TTGGGTTTACTTTGTTGGCAGTCCCTCCCCA

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GGTCTACATGTGCTCGCAAGATTGGATATTGAAATATCAGCAAGAAATTA
AATGACATAGTAGTCATTATGCCTAAATTATTGTTATTTTTTGATTGAAA
AAAGTTGAATATTTCAAATATCAAGGTAGTAGTGAGATATAATAAAGAGA
GAGTCAGTTCTAAGTATAGAATTGCTGATTAGTTAAGCTCTGTTCTCCA
ACATTTGGGGCCACATTGAAGAGACCATGTAGCTGCTTTCAGCCTCGGTTT
CCTCCTTTGCAAAATGGGGATTACACTACCTGCCTCACAGAGATGTAAAC
TTATGACATGTTATCATGATTGCCAGGGCCACCTGTTTTCTTTTAAACA
TTGAAATCACTGTGCCTGAAACAGGGATTTCCCTGCCCTTGTGCAAGCT
CCAGAAACAGGAGTCAGCCTGAGTCCCGCAGCTAAGAACGTGGATTCTGG
TCATTTTCTCATAGCGAACACACTTCACAGGTCCTTCAAGGGAGTACATT
TTCCTATAACTACCTTAATCTCAGTTGAAGCCTCGTTTCTTATTTTGCA
CTGTGGCCAAAACTAAATCTCATTCTTTTACGTAACTTCAGCAATTC
AATAATAGTACAGTCATTTTATGTTTCAACTGAACCAAGTCAGGGTTCCA
CTCCTGCCTCCCTTTCTGCTCTGAGGACATCCATGAAGTGAGGGGGTCT
TATGTAGCCTGGAGCTATTGGTGAGGGGCGATGGGTCCGTGGTGGTCTTG
GGGAACCTGCGGGGCTGTGTCTGGCTGGTCTGGTGTCTGGTGATTGGCCTT
GTTCCACGCGGTTACGCTGCAGGACAGTTCGTGTCTTCTTGTCTTAAT
GATCAGCTTTTAGGCTCACGGGCTGTCTCTGCTGAGATATGGAATAGGA
CAGCCTCTGGATCTTCTTTAACTCTCCTGGGGCCACAGGGGACTCTGTT
TGTGTCTGTGCCACATAGGATGATTCTGCCAGACCTTTGCTGCCATTT
CTTGCTGTTCTGCTGTTTTAGTCTCTGGAGGGCTTGCAGTTTCTTGGG
GTCCCTGTGGAAGCAAAGTCCCTCTCCAGCTCAGATGTCTAAACG
TATCTGGGTTTTATCGTCCACCCATCCCAGAGCTCAGTCTAGAGGAGGGG
GCAGCCTTCGGGTTCTCTCCTTCCCTCCAGAGCCTCTTCTTTGCACCAG
GGCAGCCTCTTCTATCTGTTGGAAGGGCTGTCTGGTTCTTGAATATAG
AGTTGCAGGTTTGAGGGGTGTAGGCTGAGGTAAGGCAAACTATCACATGG
AATAAAAATTACCCTGTGTCAAGGAACAACCAGAGCTGGACAGTTTTTAA
ATGTGAAAACCAATTTTATTTCAGGACTATGGCGAGAGGTGAAGTAAGACC
TCAGTATAGAACTGGGCTCAATTCCGAATGCAGCATGGGCAAATGGGAAT
GTATAGCCTAGGAGCAGGGTGGGAACCTGTGGATGAAGAATTACTAAAAG
GGCATATCAGGGGTGAGGGGGCGTCTGGCTACACCCACTAACTACTGTT
GCTGAAGAAAGCCCTGGTGACATCACTGGGGAATGGTGGGGGATGAAGAA
TCCAATCAGATGGATATTGAGGATAAGGGGATCTTGATAAACTGGCTTAG
GAGGGTTTTTGCTAAAACCTGGTTTTTCATAGGTAAGTCCACAGACAGGTCT
TGGAGAAAGTTCAGGGACCTACGGTTTTGTTGCGGCAGATGCTTTGTCTATC
TGTACACTGGCACTGTACCTGGCTTTCTTTAGTCCCTCCCCCCTTT
TTTTTTTCTGGAGTAGTTTGGGAGACCAGAGGAGCAGGGAGTTAGGGAG
AGTAGTCAGAAAAGGCCAGAGAAAATAAGGAGGTGTCTGTAGGGAAAATC
CTTAAATCCTCTAATTAAATTAATTTAATTTATTTATCTGGGACAAGGTC
TCACTCTGTTGCCAGGCTGAAGTGCAGTGTTGTGATCTCGGCTCACTGC
AGCCTCGACCTCAGGGCTCAAGCAGTTTTGCCACCTCAGCCTCCTGAGTA
GCTGGGGCTCACAGGTGTGCACTACCATGCCCCGGTAATTTTTGGGTTTTT
TTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTTGTAGAGATGAGGTTTCGCCATG
TTGCCAGGCTTGGTCTCGAACTCCTAAGTGATCCATCCACGTCGACCTC
CCAAAGTGCTGAGATTACAGGCATGAGCCACTGTGCCCGGCTAAATTTCT
CCAATTTTTAAATGCTTCCCTGTTCCCTGTTCCAGATTTGGGATATTGAC
TGCTGTAAATCAGCGATTTCTCCCTGTGGAGAGGTAGCCAATAGGAAGC
AACAAGAGTGAGGAGTCTTATATCGAAATAGAGGGTAAGAGAAGAGACA
GATGTTATCTTGGCAGTGATTTAAGAACAGCGAGTCTGTAAGCAAAGCAA
AGCAAGGCTCCAGGTGCTGAGAAACAATGGCTTTCTGGGGAAGCGTCTG
TGTTTCAGAACCTTAAGTTGGAACATCTCTGAAGATGTTTGCCATGAAGG
TTTTCTTCTGAAGTTGAGTCTTTCATCACTAGGTAGGCGTGTGTTTGGAGT
CTCTATCAAACAGATCCTGTGTTTTATTAGGAAGCTGTGGTTCAATAAGCC
CCATGCTAATTTTGCAGGTAGCAGGGTGGCCCTGGCCTGACCCGGGACA

FIG. 3 (36 of 52)

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GAGTGGCTGTCTCCCTCCCTCAGGCAGGAAACTCTCTCCTGCCACCTAGTCT
CTGCATACCCACATTTCAAGGGAGCTTCTGGGTGGTGAGTTTACCAGACT
ATGGTCTGAGGTAGAGTTAAGCAAAACAAACTAACTGCATAAAGAAAC
AGAAAGAAAATCAGGTGTTATAAAAAACAATTTGGCATTGTGTTGTGTTTC
AGCTCCGTGTGCGATTATTGCTTCCACAAATAGTGCCGATATGCACCAGG
CACTGTTGTAAAACCTGAAAATATGTTTTTGGATGTGCCAGTCTGTGAGT
ATTAAACGATGGTTGATTTGAAATTTGCTATGATTTCATATTTCTGGGGGT
AAGATGCAGGATTTCTTTGGGGGGCCTACGATGTGGCATTCTAGAATTCT
CAAAGAATCAACCCTGGTGGGACCAGGAAGAGCTGAGCTGAGGCCTCTCT
GCTCATGTGTACTTACTGGAGATCATGGAGACAGGTGAGCCTGAGTGCAC
GTCTCACCAAAGCCACAGCAGAGGGGGAGGAGGCGGAAAGAGAGCTCTCT
CCATTTCTGAGAAGTTAATGGTAACAATGGCATACATACCTACTTTACAG
TTGAAATTGGAAACCACAGCATTAAAGTGTTCCTAATGAAATTTGGCAATT
TGGGAGTTTTCTGAGCTGCATTGGATGTGGTTTTGTCATGCTGTTAGGATG
AGCAAGAGATGAGGAGAACATCTTCTTTTGGAGCTTCTCTTGGACGTG
GGTCACTCCCACCTCATGGAATTAGAAAGCTTAGACCTAGACTTGAATCTC
ACCTTCTCAAGGTGCTCCCGGGCAAATCACTTAAGATCCATCTTCTTCTC
CTCCTGCTCCTTCTCCTCCTTCTGAGTTTTTTTTTTTTCTTTCCAAAATTC
AAATGACACGGTACTGGTAGAAGAAAAGGTCCAAGTCTGCTTTTACAGCT
CCCCTCATCCCCAAATGTACTCCGACCCCAAGATGACCATGTTATCATTT
GATTGACATCCTTCTAGTTTCAACTCATTTCTTTGCATGTATATGCACGT
ACATATACACTATTTTATTTTGGCAGGGGTACCGTTTAGCTGCATTAAT
TTCTTATAAAAATAATCTATATTTACTTATGGTTTACGTAAAAACAACATAC
ACATGTAAAGTGTATAGCTTGATAAGTCTTCACTGTAAACCAAAAATAAAA
TTCGAAGCCCCCCCCAACCGTCTGAATGGACCCCTCTTCTTGGCCAAGAGC
ATTCCAAAGTTAACCTGAAAAAACTAGTTCAGGTGATGGAAGGGAAG
GTTGGACATGCCCCAGTATACCCCTTCTCCCTTTTGGAAATTCAGGAAAAGC
TGACCAGCATTAACATCAACACAGACCTTATGTCTGATAGGAAACTTTGA
CAATCTATTCCCTCTGAAGCTTGCTACCCGGAGGCTTCATCTACAAGATA
AAACCTTGGTCTCCACAACCGCTTATCATAACCCAGACATTCCTTTCTGT
TGAGAATAATTTACCTTGTAACCTGGAAGCTCCCTGCTTCAAGTTCCCTC
ACCTTTCCAGATTGAACCAATGTAAACCTTACATGCATTGATTGATGTAT
TATGTCTCCCTAAGATGAATAAAAGCAAGCTGTATGTTGACTGCCTTCAG
CACAGCTTGTGAGGCTCCTGAGGCTGGGTACGGATGCATCCTTAACC
TTGGCAAATAAACTGTCTAGATTGACTGAGACCTATCTCAGATACTGTT
GGGTTCAAATATATACTTATGAAACTAATACACAAATCAAGTCATAGAA
TATTTCCATCACTCCTCATCTACCCCCAAATTTCTTATGCGTCTTTGCA
GTCAACCTCCCACCCCATCCCCAGGCAACTGCAGATCTACTTTTTGTCTC
TGCACCTTCAACTGACCCCTTCTGTGATTTTCATATGAATGGAATCATGCG
CTGAGCAGTCTTTTGTGTCTGGCTTCTTTTGCTCAGCATAATGTTTTTGA
GGTTTGTCCATGTTTTTGTGTTTGTCAATGGTTAATTTCTCTCCATTGCA
GAGTAGTTTTCTATTGTACATGTGTACCACAATTTGTATATCCATTCCAT
TGCTGATGGACATTTGATTTGTTTCCAGATTTTGGCAATTATGAATAGAG
CTACCATGAACACCCAGGTACAAGTCTTTGTGTGGACTTATGTTTTCTATT
TCTCTTGGAAATGGAAGTGTATATCAATAAGTATATGTTTAACTTTGTAA
GAAACTGACAACAAATTATCTGCGATGGTTATGCCATTTTGTTTTTCTAC
CAGCAATACACGAGCATTTTCAAGTGTCTCCACAACCTTTGCCAAAACCTGTT
TTCTTTAATTTGGACATTTAAGTGGTGTACAGAGGCATCTCATTGTGGTT
CTAGTTTTCTTTGCCCTGATGACCAATGGTGTGGAACATCTTTTCATGTG
CTTTTTGACCATTTACATATCCTCTTTTGTGAAGTGTCTGTTCAAATATT
TTTGCCCATTTAAAACATTTGGGGGTTTGTCTTATTATTGTGTTGGGAGA
GTTCCATATTTATTTATTTATTGAGATGGAGTCTCACTCTGTTGCCCAGG
CTAGAGTGCAGTGGCGTGATCTTGGCTCACTGCAACCTCCACTTCTGGG
TTCAAGCAATTTCTCTGCTTAGCCTCCTGAGTAGCTGGGATTACAGGCA
TGTGCCACCACACTGGCTAAGTTTTTGTATTTTATGATAGAGATGGGGTTT
CATCATGTTGGCCAGACTGGTTCGCAATTCCTGACCTCAAGCAATCCACC
TGCCTCGGCCCTACAAAGTGTCTGGGATTACAAGCATGAGCCACTGTGCCT
GGCCCATATTTATTTTTATTCTTTATTTTGTATACAAGTTCTTGGTCAG
ATACAATAATACCTGGTCAGATGAGATAATGAGTTGGAAAATGCTTTGCA
AATGGGGGAGAATAATTTAAATGTTATTTATTTAAGAGCAGAGGCC

FIG. 3 (37 of 52)

TTCTGTGCGGTCAC...AAGCCGTTTGCTTCTTCTGCCTTTTATAAA
AGCAGAGTCGAGCTACACAGGCTGTCTGTGTTGGCTGCTATTAGTTAATC
AGAGAGTTTTTTTTTCTTGCTTGTCAATTCTAATTTGTGACACATAATT
AGCCACAATATGTGTTTTTCTGTTGTGACACTGGCCTGGGAAACCAAGGGA
TGTTTAGAGTGGATTTCTTGATTTTGCAATAATTGTGTGTTTTTCTGCA
TCTTCTGTTAAACACAAATTCATGGAAGCAAAACATGGAAGCAAAGTACC
CTGGACATCCCCCTTCTTTATGAAATTGATTTCTCTTAAATGTAATGTT
TGCTTGTTCCTTACTTTAAAAGCAATTTAAGAGTTTATTGAGAAAGTGA
GCCCTGGAAACATAGATGCATAGAGAGAAAATTTACCACCCTCAGGTCC
CTATTGTCTTCTCTCATAAAGTGTAGTTTTCAGGGCCTTTTAGAAGTTTCT
TTTCTGCTCTGATTTGCATGTTTGTGAGTGTGCTATTTTAAGTATTTGG
ATTTGGTCTGCAATCCTATGAGAGATGGCAACAGAGTAGGGATCTCAA
GCCTGCAGGTTGTATTAAAGTCCAGCAGGGCCTTGATTTTACAACAGAGGG
TCCTTGAAGACATTCCATATATTATGCTAGGGGAGTGGCCAAGCAAACCTT
TAATGTGTCCCTATGGTGGGATATTTGGGGTTAATACCTGCCCTTCTCTT
AATTTCTTTTTCTTTCTTTTTCTTTTTCTTTTTCTTTTTTTTTTTGAAA
TGTAGTCTTGCTTTGTCAACCCANGCTGGATTGGAGTGCAGTGGTATGATC
TCAGCTCACTGCAACCTCCACCTCCTGGGTTCAAGCAATTCTCCTGCCTC
AGCCTCCCAAGTAGCTGGGACTATAGGCACACACCACCATGCCTGGCTAG
TTTTTTTTTTTTTTTTTGAACNGAATCTCGCTCTGTGCGCCAGGCGGGA
CTGCGGACTGCAGTGGCGCAATCTCGG

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CGCTCGCATCCCTCATATCCATGAGTGTCTGTGGGCCCTGCCTCTGAAA
TAAATCCTGCCTTTGTCTCCAGTTCACTCCAGCCACCCATCCTGGGGCT
GCACCCTCCTCCTTCCAAGCCCTCTCCCTTTCTTCTGCTGGTGTGCTGT
CATGTCAAGCATATGCATCAGTGCAGACCAGGACATTTGAAATGCAACCAG
TACAATTGGGCGCGGTTATGCCTACCAGTTTTCTTCTTAAACATTTTA
TATTTATGTTTGAAAGCATGCCACCTTTCTTCACTTGCCAACCTGACAGA
TTTATTAGTTGACAACATCCGCTGATAGCATCAGTAATAAGTTAATTGTT
TTTGACATGTAGCTTTAATTATTCTCATTATCATTATAGGAGTTATTC
TTTGTAAGGGTAAGTGTGTTTCCAAAACAAACAGAAATTTGGGGTGGG
CCCATTGGAGCGTGACTCATGAAATCAGATTCTTAGAAGGACCTCGGCAAG
TCTCTGGGTTGCTGTTAATGAGCCTGGCTGGCTGCCAGGGGTGTGTCTGC
CCTTTATGAGGCCACCAGTGTCAAATGCTTGCTGCCTGCAGCATTACTTGCC
TAGGTAGTGCTTGTCTTCTACTGAACTGTGAGGGATCCAATTCTTTGTGGT
CTAAGTAACAATACTCAGATTCACAAGGAATTGATTAATAAGCCAGAATG
CCAATGTATTACATTTTTGATGAAGACCATATTTACAGTGATTGTATCTG
CTCAAGCTCAAATTAGGATTAGAGTTCTGACAAATACATATGTGAGAAGT
ATGAGGTTAAATACTTGAAATTTGGACTTTCTAGAAAATCTGAATGTGA
TTGCCATTACATACCTTTCTGGGGATGATGATTCTTGTAATTTTATTTT
AAAAGACATAGAAAATAACTTAAGAATCAGATTGCTTGGCTGGGCACAG
TGGCTCATGCCTGTAATGCCAGCACTTTGGGAGGCCAAGGTGAGTGGATT
GCTTGAGCTCAGGAGTTTGAGATCAGCCTGGGCAACATGGTGAAATCCCA
TCTCTACCAAAAAATACAAAAAACAACCAAAAAGAATAAA
TTAGCTAGGTGTGATGGTGCGTGCTTGTAGTTCCAGCTACTTGGGAGGAT
GAGGTGGAAGAATTGCTTGAGCCCAGGAGGTGGAGGTTTCAGTGAGCTGG
GGTTGCAACAGTGTACTCCAGCCTGGGCGATAGAGTGAGACTCCGTCTCA
AAAAAATAAATCAGATTGCTTTATTGCTGGTTTTCTTTCTAAACTGA
GATTGGGTCCCATCATCCCCTGGCCCCCATTGGTTAATGGTTCTCCTTT
GTCTATTGAATAAAATACAGATGTCTGCTTTTGGCAACATGGTTGAATGT
AGACACTGCAGGGTCTTCTGACTCAAATGAGTAAGGCTTAGATAAAAC
ACATTTTGAAATGCATTTCTGGATGAACAGCAAGGAAAGGAGATCTCTTA
AAATCCTCTTTCTGTTCCCTCTCCCTACCCCTCCAAGTGGGCTTAAGT
AGGAAGGTGGTGAGCGGCAGGTAAACACACGTCAAAGGCAGTCTTCCTC
TCTGAGGGGAAACACTTGTATAAGCATTGCAATCAATGGGCCTCTTAAT
TATGTGCCAGTGGCAAGAGCGGTGCTGAACCCAGGGGCTGCCTCAATC
CGGGGCCTTTGAGGCAGAATAAAGTGGTCTCAGGTTGTTGGCATTTCCTT
GCCCTTCCACCCGAAGCAGACACAAATCCTCTCTGGAGGCAAGTCCCCA
ATTACGCCAGTACAACCTCCACAGACTAAGATCAATCATGTACAAGCTCA
CAGACAAAGGTCACCAACACACAGAGCAATAAACAAATTCATGAGTGAC

FIG. 3 (38 of 52)

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GTGAATGAGAATAAACACAAACAATAACCACCAGCTGGGATGCTCTAAG
CTTCAGCTGTTAGAATTCCTGAATATAGAATAAACTGCCACAATGGCAA
ACATGCATCTAGTACTTACTGTGTGCTGGGTTCTAAGAATTTTGCACATT
GTGCCAGATACCGACTCAGCTTCACACTCACCTCCTACTGTGCCCTCTT
AATTTGCACTAGATTTAAAGGTAGAAAGGAAGAGGCAGCTATTCTGTTCT
TGGCTGTGCCCTCTGGCAGCATGCAAAATGGGCAGTAACAGTGGCAGTC
ACAGGTAAGTAGCCTTCTCACAGTGTGGAGTTAAAGGCATGGGACTGAGA
CGAGCAAGGTTCTTAAAGGGACAGTGGCCAGTAGATGACCAGGGGCTACT
GGAGTGGCTGCATGGCTCTGTGGAAGCTCAGAGGAGCCTTGGGTCTGCA
GGTGCAGTAGCAGCTTTCTGTAGTTCCTGATCTCTGGGTCCCACAATCTT
CCCCGTTTTTGGCTCCTCCACTTCTAATTTTGTAACTGACTTCCCTGTGTG
TACTTCTCTCTCTGATTGAAATAGCCAGACTGCTTTCTGTTTCTGATAA
GACATTGTCTGGTACGAACACAGTAACCTATTTAATCCGATATCTCTATG
AAGGAGGTACAATAATTATTCCTATTTTACAGATGAGGAAACACAGCAGA
GAAATAAAGTCAATTGTCTAAGGTTGCACATTTAGTCAAGGGAAGGGTTG
ATATAACATATAATTATTAGAAAACATCTAAGGAAATAAAAGGCATAAT
TTAAAAATAAACTAGGCAGGTTTAAAAAATGAAGTAATCTATAAGTAA
AAAAGTATAATTGTTGAAATACATATCTTAGTGGATGGGTTAAATAGCTG
AAGAAATGATTAATGAACTGGAAGGTAGTTCTGAGGAAATCAGAATTCAG
CATAGATAGAAAAATGGGAATTTACAAAAGTACACAGGAATTATAAAAG
AGGTAAATTTATAGGGAGGCTAGAATGAGAATTAACATTGGTCTAACTGG
AATTTTGGAGAAGAGAATAGAGAGAATGAACAAGGCAATATTTAAAGAG
GTGGCTGAGAATTTTTTCAAGCAACACAACTATGACTTTACCAGTAGA
GAAAACAATGTACACTGAGGAGGATAAATAAATACTATGAACAAATTG
TAATAATAACTCAACAAAGACAAAGAGAAGATGTTAAATCAGCAAAA
AAAGAAAGTCAGACTTAGAAAGAAATGACAATGCCAGACTACTCAACAAC
AACAATGGAATCCAAATTCGGTCAAACAGTATTTCTTCATGCTAGCATA
TAGC

>Contig40

GGGAGTCCGCTATGCTCCTAAAGATTTGCACCTCTGATCTGGTTTGTAGT
TAGTCTCTTTTATTGCTTTATCCTACTCAACTAATTTTTTTAGTGCCTGT
TTTTTTTTTTTTTAATGTGTGTTGATGACTACAATCTAACTCATTCTA
CTGATTCTGGGTGCTTTAAATCTGAGCAGTCTTTCGCATTTACTGCCT
GTGATGGCCCCATCCCACCAGCTAAAGTGTGTGGCCACTGCTTACAGCACC
ATGTGATAACGAGTAAGGGAGAGATGCCGCCAGACTCTTCTAGGAGCAG
CCAGTAGGACCTTCCAGGGGTTGCAAGCAAAACACAGCAATATGTGGAGT
GTGGCAGAGGATGGCCCCAAGAGGATGTGGCAGCGGCTAGTGCAGCTCAG
CTTAGTCTGAGAGGAAATGCTGGAGAGGAGAGCCAGTCTGTACAGGCAT
GACAGCCACAAGGACTTCAACAGCTAACATGGCTGAGTGGACTTTATGTG
CTATCTCATTGAGAAAACAGGAGCAATCAGAAAGGAGTCACCTCCTATTT
GTACCCCAAGGAATTGCTAACCTACTTGCATCTGAATGATGTCCATCACTT
CCCTTCATCACCTCCTCTGGGGGCTCTGCAAGGATTTGACTCCTGCATTA
GTGATCTGTCTCACCTACGTTGTGATTACATGAACTTACTAATGTGCTA
TGTGACAACTACCATCTTAAACACAAAAACCCTCTTTTGATTCTGTGGCT
CCCTCCAGCTACCCCTGCATTTCTCTGTCCCCCTGCCCGTCTCTGCACT
CACTTTTATTTTACAGCAAACTACTCAAGGGAGTCTCAGTGTCTCCTTGG
CTCCATGTCTCCACCTTTCATTCTCTCCTCAGTTCACCTGTGTCAGGCTT
CCGTCTCAAGCTCTTCTTCACTTTTGTCTAGGGCCGCTGACATCCTCT
TTCTTGCCAAATTCAGTGGCCAGGTCCTCACTTACTCAACTGCTCAGCAT
TGTTGGGCCTGGTGGACCACATTCTCCTTCACCCACCTTTTGCTGCTCTC
TCTTCTCTCCAGATGTTTCTCTCTTCTCACTGGCTACTCCTCTTTTGTCT
CCTTTGTTAGCTCCATTTCTTCTTCCAACCTCACTGTGCTGGTGTGCCC
AGTGCTCAGTTTTTGTAGCTATTCTCTCTTTTCCAGTGGCATTCAATGATG
GTATCATGTGACCCATGGCATTATATGCCCTTCTACATGACAGTTACTCCT
GAATATGAATCTCAGGAAAGATTTGGATTATTTTTTAATTAATTTTTTTA
AATTTTATTTTAATAAATGAGGTCTCTCTGTGTCATCCAGGCTGGAGTGT
AGTATTGAGTGATGTGATTATAGCTCACTGCAGCCTTGAACCATGGGCTC
AAGTGATCCTCCTGCCTCAGCTTCTGAGTAGCTGGGACTACAGGCATGT
GCCACCATGCCTGGATGACTTTTGTGTGTGTGTGTGTGTGTGGAGACAG
GGTCTTGCTCTATTGCCCAGGCTGATCAAACTCCTGGCCTCAAGTGAT

CCTCTCACCTCAGCCTTCAAAGTGCTGGGATTACAGGTGTGAGACCAJ
CTGGGCTAAGATTGAGATTTTGTATTCAATTGACTGTTTGACATCTTCAC
TTGGACACCTAAGAGGTATCTCAAATATTAATTAACCTGGCCAAAATACA
GAACTTTTGACCCCTGCCCCACAATACTTGCCCTTCCCCAGACTTCTC
CATTTCTGTTAAATATCCCCAGTTACTCAACCTCAAACCTATGAATGCC
CTTTGATTTCTTTCTTTCCCTCATCTCCTACGTTGACGCCATCAGCTAGT
TTTGTGTCCTTTATGCCCAGAATATAATCCTCACCACCTTCTCTCCTATT
GCCCCAGTATAAGATGTCAGTTTTTCCTGCACAGTCCATTGCCCTGACCT
CCTGAGTGGTTTGCTTCCACTTTTGACATTTGTATTCTTCTTTCCCCCAG
GGTCAATTTTTCACAGCAAGAGTGGCATTTTTTTTTTTTTTTTTTTTTG
AGACGGAGTCTCGCTCTGTGCCCCAGGCCGGACTGCGGACTGCAGTGGCG
CAATCTCGGCTCACTGCAAGCTCCGCCTCCCGGGTTCACGCCATTCTCCT
GCCTCAGCCTCCCGAGTAGCTGGGAATACAGGCGCCCGCCACCGCGCCCG
GCTAATTTTTTGTATTTTTAGTAGAGACGGGGTTTACCTTGTTAGCCAG
GATGGTCTCGATCTCCTGACCTCATGATCCACCCGCCTCGGCCTCCCAA
GTGCTGGGATTACAGGCGTGAGCCACCGCGCCCGGCCAAGAGTGGCATT
TTAAAACCATATATTAGATCATTGCTTTTGTGTTTGGGAACCTCCAAGGG
CTTTGCATCATATATCAAGTTGACACCTCTCCTACCCAAGCCTGGCTCTT
TCCTGCTCCTCTGCTCCTCTCAGCCCCCTCCACCCATTGTTTCATGCTGCTTC
AGCCACACTGGCCTTCTTGCCATGCCACATTTGTGCTAAGCCACATCCA
ATCTCGGGGCTTTGCACTCGCATTTCCTCTGCTTGGCATGCTGTACCCC
AGATCTTTCATGATTGGCAGCTTCTGTACATTACGCCACCTGCTCAAGCC
ACCTTTTCAGAGGGCTTCCCTGGCCACCTCACCTGAAATAGCACCTCCG
ATTGCAACCCATCCGGTTATTCTCCATCCTGTTCTCTTGCTTGGTGATTTT
CCATCACTGATGAGGAAATGAACCATGGAATGCTAGGGCTGATGACCAGA
ACTTTCCCCCACCCCCACATTATTACAGAGGAGGAAATGAGGTTCGGAGGT
AAGATGGGCCCAGGATTTCTACTCCCGCTGGACTGCAGGCACAGCACTG
ACCTCAGCTGTGCTCACTCTTGGCATTACCCAACCTTCTATCTCCAAC
TGCCCCATTTACCAGAAAGTGAAATGTTCTCAGAGACGGTGAGCCACCTG
ACTTGACAGCAGCCCAGGGCCCCCTGGCACCTGCTTTCTTCTCCTGC
CATCCTTTCTCTCCAAGACCTACCTTTCCCTGTGATTCTTGCCACATG
CTGCATTTTCATGGTTTTATGACCTGATTTCTGAGAGGGATTGAATTTTC
ATGATTATTATGTAAGCAAATCATTATGCTTATACAAATGAGAAAAGGA
GTGCTTCTGACTTCCCAGGGACAAAATCTTGTCACCTTGGCTTGCTTTCA
TATTGCTAATTAAGGACCCAGGATGTGGGTGAGATGTGCTAAAAGCTGAG
AGGAGGCTCTGGACTCTGACTATGGGCCCCACACCCCTGGGCAGGCATCAC
ACTAGTCCTTTAGGTCATCCTCAACCCAGCTTCCAGTTGAATCAGATGTT
TGTGAATAACTCAGCAAGGCTGTATGGGAAATGAAGAATGAGGTGGGGAA
GAGGCCTGTGAGAAAGACACACTGACTTACCCCTCTACCTCTAACTAGGG
TGTTGTAGCAGCCACCCACCCACCAAGTCTGTCTTCCAGACCACGTATGC
TTTCTCCACCTTTGCATCTTTTATCTTCTGCCAGCCCAGATGCTTGCTG
ACTCCAGCCCAAGCCTATAGGATAAGCTACAGCCTGTCCCTACAGACTAC
GCATTGCAGAATCTAAGACATCAAGTCAAGTTCGGAAGCACTTGCCTTCT
CCTCTCCAGGTACACAGGCTCTCCTGGAAAGCTGGTAGCAGCTGTGGAGG
TGTGGTGTGTTACCTGCTGCAGGTGCAGAGAAGTTGACTTCACAGCCCTT
CAGAAAGACTGCCTTCTTCCAGTTGTATTTGTGTACTTGCTTGGGTGTGG
GGAGGATTCTCAGCTTTCTCCACTCAAATTATCAGACCCCTTCCATTTAG
TGGTAGACCATTTCCCTCGTCCAGGCCAAGGGCACATAGTACAGAGAAAT
AGGGAGTTGTTACCCAGGGAGAGAACTTGGCTCTAAACCTGTAATAGAAA
GGTCAGTTCTGGTCTGGAGGGTCAATTTTGATCTTTGGCTCAGATCCAGG
AATTGGAACCAAGGCTTTTGAACATTTTAATGCAGGGGATTAAAAAATG
ATACGAGTCATTACGAATATATTTGCTTAACATCTAAAGAGATCCCTCA
AAACACTAGAAAAAATAAGAACAAAAATCTAATAAAACAAAATTTGTTAA
ACACATTTACCAAATTTTTTTTTTTGGTAAAAATTCAAATGTCATAAATA
AAGCTAAAGTTCTCTTGATGACTCGCTCCTCTGCCCTATTCCACTCCAA
GTAACCACTATTATCAGTCTTGCCAATACCCCTCCAGACCTCTCTACCTC
TATATACCATTAGAAGCACATGGTTTTTGCAATTGAGGATGTGCAGTGT
GTTTTACGTAAATGTTATCACTCTGTTCTTGTTCCATAATTGCCTTTTT
CTCTCAATGATTTGCTTGGCTATCTTCTATTTTCTAGTACATCTCCTTTC
TTTTTAACCTTACCATTGTTTATTTAACCTTGCCTCTATCAACAGATATGT

FIG. 3 (40 of 52)

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AGGTTGTTTCTAGTTGA. TTCATTAAGTATTTATAAAACAACGCATCAGIA
BATGTCCATAAATTTCTTTACGGAAGATGGCAAGTAGTGGAATTGCTGAG
CCAAAGAACATGTTTAAAAAACCACAAAAAACTAGACGCTACCAATTTTC
TCTCCAAAATGGCCATACCCACTTACCCATACAGAGATGATTTGGAATCT
GGCTTCCTCACAAGGTGAGATGCCTTCACAGTTTCATTCTTCCTGGCATG
TCTTCCCTTTTGTATCTGAGAGAGCTGGCAGAATTGTGTCACTAAATCAA
GGATAGAGGGGTCAAATGACAGCTCAAGCTCACAGGCACCTCTGCTTTCTT
CCCAGACCACCTGCTTTCTGCCCACAGCTCTGTTCCATCTTATAGAATG
GTTGCCACTTGGGTGTCTGCTCCGACAGCCATGTATCCTTTGCACTGCA
GTTATGAAGCAGACAGAGCTAGGAGAGGGGCTTTGCCAGCCTCTGCCCTA
GCTTGGAGAATTTCAAAGAAGGAGGGTATTGAGAGTGAGCTGCCGAAGAC
TGGCAGCTCCCTCAACTCAACAGTTGTCCTTCCACAAGAAGTCAGATACA
TTTTTTTGGGATAAAAATATTTAAAAATTATTATTTTATTTCTGAATAATA
TATTTACATGATTCAAAAATCAAACTGTAGGCCAGGCATGGCTGCTTATG
CCTGTAATCCTAGCAATTTAGGAGGCCGAGGCGGGAGGATCACTTCAGCC
CAGGAGTTCAAGACCAGCCTGGGTAACATAGTGAGACCCTGTATCTACAA
AAATTTAAAAACAATAATTAGTTGGGCATGGTGGCTGATATGGTTTGGCT
CTGTGACCCAACTCAAACCTCATGTTGAATTTTAATCCTCAATGTTGAGG
GAGGGTCTGGTGGGAGGTGATTGGATCATGGGGGTGGGTTCTCCCTTGC
TGTTCTCATGATAGTGAGTGAGTTCTCACAAGACCTGGTTATTTGAAAGT
GTGTAGCACCTCCCCCTTCACTCTCTCACTCTCCTGCTCCGCCATAGTAA
GATGTGTGTGTTTTCCCTTTGCTTCCGCCATGATTGTAAGTTTCTTGAA
GCCTCCAGCTATGCTTCTGTACAGCCTGTAGAAGTGTGAATCAGTTAG
ACCTCTTTTCTTCATAAATTACCCAGTCTCAGGTCAATCTTTATAGCAGT
GTGAGAGTGGATGAATATAGTGCCATATGTTTGTATTCCAGCTACCCAG
GAGGCTGAGGTAAGAGGATTGCTTGAGCCTGGGAGTTTAAGGCTGCAGTG
AGCCATGACTATCCACTGCTCTCCAGCCTGGGTGACAGCGAGACCTTGT
CTCCAAAAAATAAAACCCAAACTGTGTAAATGTGTTTATAAAAGTGTC
TTGCTCCACACCTGTCCCTATATATCTTATTCTCAGCCTCCGACAACCT
ACTTTATTCAATTTCTTATGTATCTTCCAGAATCAAAAAAAAAAATCAAA
TACAAGCACAGTGAATGTATTGCCCTTCTTCCCTCCCTTTTGTTACAT
CAGAGTTAGCATATCATAAATACGGTCTGCATTTTCTTCTTTTTCAGCTA
TCAGCATGTTTTGGAGAGGATTTTCATATTCGTGCAGACAGCATGTATTAG
TCAGTCCTTGCAATTGCTATAAGGAAATACCTGAGACTGCATAATTTATAA
AGAAAAGAGGTTTAAATTGGCTCACAGCTTCGCAGGCTGTTCCACAGGAAG
CATGGCAGCATCTGCTTCTGGGGAGGCCCTTAGGAAGCTTTTACTCATGCA
GAAGACAAAGCGGGAGTGGATGTCTTATATGGCAGGAGCAGGACTGAGAG
AGAGAGAGAGAGAGAGAAAGGATGCCACATACTTTTAAACAACCAGATCT
TGTGGGAACTCTGTACGAGAACAGCACCAAGGGATAGTGCTAAACCAT
TCATAAGAATCCACCCCATGATCCAATCACCCACACACAGGCCCCACC
TCCAACATCGGGGATTACAATTTGACATGAGATTTGGGCTGGGACACAGA
ACCAACAATACCAGAGTGCTTTCTCATTCTTTTCTATAGCTGCCTAGTA
TTCTATGTCCTTTACTTCAATTTAGGCAGTCTCTTGTTGATAGACACTTGG
GTTACTTCCAATTTTCTTATTACAAATGATGTGCAATGAATAATTTTGA
TCATTTTCCATTTACATGGGTTATGTCCATCTGTGGGATAAATCTCCAG
GAGTGAAATTGCTGGATCAAAGGGGAAGTGCACTTGTGATTTTCATAGTT
AGCAAATTTGTTCTATAAGGGTCATATCAATTTATAGTCCCACGCGTAA
TATTTAACAGTGGGGATTTCCCGACAGTTTGACCAACAAGGTCTGTTGTT
AAACTTTTGATTTTGTCAATCTGATGGGAAAATACTAGTATCTCAAAGT
GCTTTTAATTTGACTTTCTTATTACAATGTTAAGCATCATTTTACTCTGC
CCAAGATCAAATAGTATTTTCTTTCTGTGAACAGACTGTTAAGATCCCT
TGCTCTTGTGTTTGTGCTGATTTTGTCTTTTTTTTTCAAATGTTTTGAGG
CAGTTCTTTACATGTGAAACAAGTTATCTCTTTATCTGGGGTGTGAGTTA
CAACTACTTTTCTCTGGCTTGTGTTTGGCCTTTGACTTTGCTTCTGGTGA
TTCCCGCAATCTGAAAGTGTACTTTTGCATCATTCACTTATACACC
CATGCTCTTGTTACGCTGGTTCCTCTACCTGAGGGCTTTTTCTTTCTG
CTTCTATCTGGGAACATTTTTTTGAGAGAGAGTCTCACTCTCTCGCCAG
GCTGGAGTAGTCAATGGCGCATCTTAGCTCACTGCAACCTCCACCTCC
TGGGTTCAAGCAATTTCTGCTCAGCCTCCCAAGTAGCTGGGATTACA
GGAGCCCACCACCAAGCCCAGCTAATTTGTTGATTTATTTATTTATTTT

FIG. 3 (41 of 52)

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TGTAGAGATGGGAGTC...ACTATGTTGCCAGGCTGGTCTTGAAGTCC...
 GGCTCAAGCGATCCACCCACCTCGGCCACCCAAAGTGCTGGGATTACAGG
 CGTAAGCCACCATGCCAGCCCATGTGTGGAAATCTTCTGTTTATCCCTT
 TAGGCTTGATTCTTATGTCGTTCTCCTCCCTCCTTCTGGATACTCCTCT
 TGTCTTTTATCTTACTCTACTTGTGATGTTACCTTGTCTGCTTATAAC
 TAGCTGCCTCTCCTATCTGAGGAGGGACTTGTGACTGTTCTCATCTCTGT
 ACTCCAGCTCCTAGTACATAGCGCTTGCTCAACAGATGTTTGGTGCAAT
 GATAGATAAATCACTGGTAGCTGTTACTACCAGTCTGACTCCCTGCAGT
 GCTTCAGCTGATCCTGTTCCAGATGTGCACTGAATATCCTTCTGTTGAAC
 AACAGAAATAAAGGGGATGGGTGAGGAGGATAGTCTTCGGTGGCCAAGGA
 TATTTTATAGTACTTTGCAGCACTCAGCAATGAGGAGTGGGCTTTAGTCC
 CCCAAGAATCTCACAGCCCTGGGTGTCTTTACTGTTTCAGTGTCAAATCC
 AAGACAAGTCAATGATCAGGAAAGACCATTTTTTTTTTGTTCAGTGAAGTT
 TATTTTCAGAACTATTGAACAGTATGATATTTGGTAATTTCAATAATATTC
 CCACCTTAAATGATCGGAGCAGATATATTTTCAGTCGTAATTAAAGGACA
 TGATTTAAAGAGAGCACACCAGTCCAAATTGAAATGATTCCATAGCTATT
 AAAAACTAGGGTTTTTACAGACAATGATACTTTTTTGCCCCCTTTGAAT
 AGATTAGACCAATGAATAAAACAAACAAATAAATAAATAAATAGGG
 AAGCGGTTGCTCATCAGAATGTGGGAGCGAATGACAGAGGGTTTCTTAGA
 ACCAAATGTGGCCGTGGTTTCTGTGAGCGTGCTTTAAGTGAGTAGGAGA
 GGTGAGAGAGGCTGGCTCAACAAAAGGGCTGGGGATTGTCCCTGAAGAA
 CCAGAGCTGANTTNCATCAGGAGTAACANAGGTAGATAG
 >Contig41
 CCGCGTTGAGGTTCCACGCAGTTCAAATTATGTCCAATTATCAACATTAA
 TGCACATTTTCAATAGAACCTGTTCCGGCTTTTCTTAGGAGGGGGGGCGGG
 GAGACGTTGTTCTCTGGGAATAAGTGTACGCAGGAGGCTGAGAAGGCTTC
 ATTCCATAGCATTCACTTACCTCCAGCTGTAGAGTGGGCTTATCATCTTT
 CAACACGCAGGACAGGTACAGATTTTTTTCTTTGAGGCCCAAGGCCACAG
 GTATTTTGTCACTTCTTCTCTCTTGTACAAAGGACATGGAGAACACC
 ACTGAAGAAAGAAGGGGGTCTTGTGGTTAGGGACACAGCAGTGCAGGGTC
 ACCCCAACCCCTAGGCCCATGAGTAGGATACATGTAATTTGGTAGCCTC
 TGTGGGAACCCACAGTGAGGTTCTTGGCCTAAGACACAGGATAACTTGA
 CTTCTCACAGACAATAGCAGGGTCATTTTGTTGATTTAGGGTTTCCCCCTC
 AAAGGCCTGAGGGTTTCTCAGAGCCTCATAGCAGTAGGAACGGAGAATGA
 AAGAGGTTCTACATTTTAAATGCTGAAGGAAGGAAGGAAGGAAGCCATTG
 TGTCACTGGCTGGCAATGTGCCATCCACAGGAGCGGAACAACCTTGATCA
 ATGTGGAAGGAAGGAAGAGGTTGAGGCTGTACTTCTGCCAGAAATCAGG
 CACCAGAACTGTTTCAGGAACAGAGAGTAGCCCATGGGAAGAACTGGGA
 GAGGAGAGGCTGAGCTGGGAAAGTGGCTCCAAAGAGAGACACTCATTTTG
 ATCTTCTCAGTCAACAGCAGTGTCAATTGGAGGCCCTGGGATCACTCTTA
 CTACCCGATTCCAAAGAAACAGGATTTTCTTGGCCTGGCTGAGAGCAAAT
 AGCTTCCCCCTGAGTGAGGCTGTCTTCAAAGTCAGCAGCCTTAGTTGCC
 CACACTCCTGTGCAGAGGCTTTGGCTACTGTGGCAGATGCCAGGCAGAT
 CACCACAGCTAATGATGGGTTCAACGCACTTGAACTTTTGGCCGTTACA
 GCGGAGAGATATAAGTTCTGCTGGGCGGTAAATTTCCCTACAAGGAAC
 CACCTGGCATTGGGTGGGACGGATGTTGGGGCAAGGGGGGAAGACTGGGG
 AGGGGGATGGACACATTATCGCTCCAGCACTCTTGTTCAGCCTCAACAA
 CAGGAAGAGAGAAACCCACAGGCAGTTAGGCCATGTCCATCAAATGACCCC
 ATATTGTGGAAGAATTGACATTGCACTATGCCAAGAGACTTGGGTGGAC
 ATGGTCTTGGGAGTGCTTGAGCCGTCTAATTTCTCAGGGTCACACTCTG
 TTAACAAATGCACTGGCCAGTGCAATCAAATGTGCCATTTCTAGGACCAA
 AGTTTGTATATTCCTTTTTTAATATTTTTTTTCACTTGTGTTGATCATTTG
 CCTTAAATTAACCTTTCTACTTTGTTTAAACATGGAGAATTAGCAAGCTG
 CCAGGAGGCCAGGCAGGGAAACCAGGATGTTTCCATTTACCTTGTGCTC
 CATATCCTGTCCCTGGAGGTGGAGAGCTTTCACTTCATATGGACCAGACA
 TCACCAAGCTTTTTTGCTGTGAGTCCCGAGCGTGCACTTCAGTGATCGT
 ACAGGTGCATCGTGACATAAGCTTCGTTATCCATGTGTGCAAGAAGAT
 AGGTTCTGAAATGTGGAGCACATGTTGTTTAGGTATAAATCAGAAGGGC
 AGGCCTCTGAGGCGAGGTGGCAAAATTTGATTTCTTGGAGGACACCTGA
 GCATATACGGTCAAAGTCTGATGACAACACCAGTAGGGATGAAGCTGGGA

FIG. 3 (42 of 52)

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GTGGGGTGGCTAAGAACTGGACCTGACACTATTAGACATGGGTTCC...
CTTCAGGTCCTATTACTGCTCACTGTGGCCGAGCAACAGAGCTACTTAGGT
AAAATGGTGATGGTCATAACACTAGCCACAGGGAGGTTACGAACCTCTG
GTGACAATGTAAGTGAAAGGCCCTGAGAAAGAGTGAGGGAGTTGCAAAT
GTCAGTAGCCATCAAGATCTTCTTTAAGAATAGTTTCCACTAAAGAGATG
ATTGCTTTGGTTTCCAGCCTTCTTTGTTTTGTCTCCCGCTGGGCCTTCT
ACCTTTAAAGGGCTTTGGCTCTGGGGGAATTGAGTTGGCTGGGGCTTGAT
GACTTCCAAGAGGACACAAGTGAGATCTACTGCCTGCTCTTGGCTAACT
ACCTTCTTCAAAGATGAAGGGAAAGAAGGTGCTCAGGTCATTCTCCTGGA
AGGTCTGTGGGCAGGGAACCAGCATCTTCCTCAGCTTGTCCATGGCCACA
ACAACCTGACGCGGCTGCCTGAAGCCCTTGCTGTAGTGGTGGTGGGAGAT
TCGTAGCTGGATGCCGCCATCCAGAGGGCAGAGGTCCAGGTCCTGGAAGG
AGCACTGCGGAGAGCGAGGGAGGGAGCCTGGTGAGGTGGTCTCTGCCAG
GAACCATGCTTTGACATCAGAGAGTAGAAAGCTCAGAGAGGAGGAAAGGG
CTTGAAAGAATCCCGAGCTTCTAAAGATCATCCCTCTCTGGGCCAGGCGT
GGTGGCTCATGCCTGTAATCCCAGCACTTTGGGAAGCCGAGGTGGATGAA
TCATTTAGGTGAGGACTTCAAAACCAGCCTGGCCAACATGGCGAAACCCC
TTCTCTACTAAAAATACAAAAATTAGCTGGGTGTGGTGGGGTGCACCTGT
AATCCTAGCTATTGAGGAGACTGAGGAAGGAGAATCGCTTGAACCTCAGGA
GGTGGAGGATGCAGTAAGCCAAGATTGTACCACTGCACTCCAGCCTGGGC
AACAGAGTGAGACTCTGTCTCATAAAACAAAACAAAACAAAACAA
AATAAAATAAAATAAAATAAAAGATTATCCCTCTCTGAAGCTCAAGGAG
GTTAAGGGTGACTCAAGGGCACACAGCAGGTAGAGGCAGACTCAAGAT
TAGAATGTGGGCTTTCTGACACCTTACAGGCTATTCTTTTAGAATAAATC
CCATTTCTACTTTGTTTCTTTTTTGTACATGCCCACTACACCATA
ATGTATACCTTCTCTATATCTTTTTGTATCCCTAATGCTGTACACTATG
ATTTGCTTTTTCATGCAGATGACCATAACATTTCCATTACCTATGCTC
ACTCAGCAAGTATTCAATTTTCTACACTGTTCTTTTTTTTCTTTTCA
TAACACTGTCTCATAGGCATTCTGCAAATCCTGTGAGAGTACTTTTGTG
AAATGTTACCACTTTCTCTTATTGAGAGAAGCTCCGTATTAAGGCTTCA
CTGAGGTTGCCTTAAGGCATGATAATGGTTCAAAGGCTTGAAAGACAGTT
AAAGAGACCTGTAAGTGACAAAAGAAAGTTGAGCAGGAGAGAATTTCT
GCCTGGAGCAGAGCCAAGCTGCTGGAAGAGGCAATGGGGGCAAAGGCCAG
GCAGACAAGCCAATGGGCTCCTCCACAGCTGCAGCCAACAAGTTATGCC
AGTCTTAAAACTTCTAAAGAAATATGTTTTTAACAAGATTGAGGACTGGA
TTATGAGGCTAGGGGAGGCTATCACAACCTGGAATAAAATAAAGCCAGAG
AAAAGTGGCTGCCTTCCAACCTGCACAACCTGACCTAGCTAGGCTGATGGC
TGGGCCACCTAGGAAGGCTACTGAGCATCATATAAAACAGAAGGGACAGC
AGGAATATAACATGGCTCTTTGTAAGGATGAGTCTGAAAAATGACCATT
GCTGCCCCAATGCCCTTAGCTACAACCTGAAAATATTTGAGAACTGGAGGT
TGCAGGATGCTGGAATCTCAGAGATCATCCAGCTCAGCCCTTTATTTTC
AGATGAGGTCCAAAGCGGGTAAAATGACTTGTCAAGGTCAAACAGCAAGT
GAATGGTTTTCTTTCAAGTCTCAATTCATCTTTTGTATATCATCTAT
GTCTTGTGTTATAAGCTTCAACCCAGGTAGCAAAAACTATTCTACTCA
AAAGGGGTAGACATATGTTAGTTCTCAAGATCATCTCTTGGTTTCAGAGT
TTAACTCAAGTGATTGGCATAGGCTGAATCCATCTCTTAAAGGATAATC
AAATTTATGTTGAAGACTTGGTTGTCTTCTACTATGAAATGGGAAACAT
TATCACTACTCCTCCCCTGTCACCACCAAGTGTGGCCACCACCACCAACG
TTAGTGAGTGAAGTGTGGTATATGATGACCAAGTGGCCAGGTGAGCAAGT
GGTGCAGCCTGTGTCTCACTGGAAGAGGTTAAAGTCTTTCTAAAACAAA
TACCATGGCATCAAAGTGGCCCGAAGTCCCTTCTTTGAGCTTTCCCTGT
GTTAGAGCCCTTCTTTGGGTGGGAGTTAAACCATAGTCTTACCTTCAT
CTGTTTAGGGCCATCAGCTTCAAAGAACAGTCATCCTCATTGCCACTGT
AATAAAAACAGGGACATGTCTCAATTATGTCTTCTAAACAGGTTTATTTT
TCCTTCCCTGTGTAAGACTTGACTGTTTATAAGAACTGCAACAGCC
TGCCTCTCAAAGCTGCCTGAAACACCTGGCAAGTTTCAAGTGATATGCG
CAGAACAGTCCAGAAGGCAGATTCTAGGCCTGGCAGGTGGGCACCTGGG
TGCTCCCTGTTGGATCTTGAGGCCTAACCTCTAGCCAGCAGAGTCAGCT
AAAATCTGAGCTCTCCCTCTCCCTCCAAGCCACACTTTGCAAAGGGATT
CTTGATTTTGGGCTTGAATCTTTTCTCCCACTTTGCCTCTGCAGGAAG

FIG. 3 (43 of 52)

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CCCTTGCAACAACACA TGGATAGCCTCCAGGTCCCAAGGCTGGAGC
CTTGTAATGGGAAAGTAGTCTTTAAATCAGATTTACTTGGCACCCCTGTTT
GCCACTGAAAGAGGCAATTTAGGGGAAAAATCTGGTCTCCAAGCACAGAT
AACACTCTACTCTTGAAAGAGGAGACCTGCTCATGTTACTGGTCTCAGCG
TCTCCACTGACCTGTAATAAGCCATCATTTCACTGGCGAGCTCAGGTACT
TCTGCCATGGCTGCTTCAGACACCTGTGTAAAAAGGAGAAAAATGAGTGAC
TTCCCCATGACGGCTACGTTTCATGTGTGATTCTCTCAGCATCCAGTGCA
TGGCAGTCATGCAAAGAAATGATCTCTGAGTAAATGAATGAATGTGTGAA
AGAGAAGTCCTTTGGGTCTAGAGAAAAGCATTTGCTAAACCAAACCCCAA
CTAGCAATGTATTGGCTAGGAGAGCTGGAGCAGAGGCTTTGACACTAACC
TTTAGGGTGTGAGTGTAGATAAGCAGTATCCATTCCCAGAATATTTCC
CGAGTCATAAGCATTATATTACACCTGGCATTTTTGCAAAAAGCTGAGAG
AGGGAGGCAGAGAGGGAAGGAGAGGAGAGACAGAGAAAGAAAGAGAGAG
AGAGAGAGAATATGCATACACACAAAGAGGCAGAGAGACAGAGAGACTCC
CTTAGCACCTAGTTGTAAGGAAGATTAAAGTCATACTTGAGCAATGAAGA
TTGGCTGAAGAGAATCCAGAGCAGCCTGTTGTGCCTTGTGCCTCGAAGA
GGTTTGGTATCTGCCAGTTTCTCCCTCGCTGTTTTTATAGCTTTCAAAG
CAGAAGTAGGAGGCTGAGAAATTTCTCTGTTGAATACCTGATTTCACAAT
CAAGTTAAAGGAAAGGGGAAAAGAGTATTGGTGGAAGCTTCTTAGGGGAG
GGGACTAATAAACTGAGATAATTCTCTGGTTCATGGAAGGGCAAGGAGTA
GCAAACATGACACATTTTGCAAATGTATCACCATGCAAATATGCATTGT
TTTCCTGACAATCGTTGTGCAGTTGATGTCCACATTAAATACTGGATTT
TCCCACGTTAGAAGAAATGTTTAAATTTAGTATATGTGGGACAAAGTGAA
GACACACAGATTTATACATGCACATACTTTTCTTCATTCACTTCTTTGTA
CTTAAGTTTAGGAATCTTCCCACTTACAGATGGATAAATGGGTACAATGA
AGGGCCAATAGCCCTCCCTGTCTGTATTGAGGGTGTGGGTCTCTACCTTG
GGTGCTGTTCTCTGCCTCGGGAGCTCTCTGTCAATTGCAGGAGCCTCTGA
GGAGAAAATTGACCTTTCTTGGCTGGGGCAGAGAACATACGGTATGCAGG
GTTCAGGCTCCTGACGGAGTTGGGGCAACCCTGGAGATAAGCTCACACAA
CCCTGCAAGACCAGGTGCTGTTACCCTAGCCAATCTCATGGATGAACCAG
ATCAATGCCAGATGAGCTCTGCCTAAAATGATTTTTTGGTGAACCTCTGAA
AAGTGAATATTGTTTCTGTAAGAATATCCATCTGAGACTCTATCTCTTG
GTAATACCAAGATTATCAGTTTCTCTTTAACCGAGACACCAGCAAAGTG
CCTGCTCCAGGGTAATGCCAGGGGAGCCCTCCATTGTAGAATGAATGA
GAGTCCAGGTTATGAACAGTGCCTGGAGTGTAGGAACACCCTCCTTTGCC
TCTTTGACAGGTCTGCATCATAACACTTTTTTTTTTTTTTTTGGAGACAGAG
TCTCACTCTGTGCCCCAGGCTGGAGTGCAGTGGCACGATCTCGGCCCCCT
GCAAGTTCCGCTCCCGGGTTACACCATTTCTCCTGCCTCAGCCTCCCCA
GCAGCTGGGACTACAGGCACCTGCCGCCACGCCCCGCTAATTTTTTGTAT
TTTTAGTAGAGACAGGGTTTACCATGTTAGCCAGGATGGTCTCGATCTC
CTGACCTTGTGATCTGCCCGCCTCGGCCTCCCAAAGTGTTGGGATTACAG
GCGTGAGCCACCGTGTCCAGCCTGTAACACTTCTTATAGCACTGAGTTGA
AACCTTGCTCCTCTGGTTCTCCAGGAACTGAAATCTTTTGGAGCCAA
GTCTAGCACAGTGCCTGGCATGTACATTCAAGGTGGTAGAGTTTGCTGCTT
GAATGGGTGAATGGGAATTTGACAGCATTTTTATTCAAATTAGTATGTGC
CAGGTATCGTGCTCGCTCTGCATTATCCAAGGGAGTGAGCCTCTGTGCAA
GTATTTGAGACACGAGGGAAATAGGTTCTACTGTGGGAAAAAGAGCATTT
CATGGACTTGCTCTCCAAGCAGCCTTCTGATTTTTAATTTGGCTCCCAGT
ATCTTGATATCAGGAGTCAGTCACAAGAACTCCATCTTTAGTAAGTTATA
TTTTCCACAGGAAATCTAAAAGCTGTTCAACATGTTAGTTTCTGTGAAT
TTGATAAGCCATAATCCATTCTTAACACTGAGCCCTCCTGAAATTTGGTG
TCTGGTCTCTGCAGATAGCTAAAAGCCCTGTCTGGGTGGCCTAGGGACTCC
TCTGTTTTGCTCCACAGGATCCACTTTGCAAATTAACCACTGGTTCTCC
CGTTGTAGGAATGCCACCTTCTCAGAGCCTGTCTTCTTCTTCTTCTTCT
CTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT
CTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT
TCCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT
CTCCCTCCCTCCCTCTCTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT
CTTCTCTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT
CTCCCTTCTCTCTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCTTCT

FIG. 3 (44 f 52)

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TCTACCTTTATCCCCC...GCTGGAGTGCAGTGGTACAATCATGCATTCA
TGCATGATCACAGCAGCCTCAAACCTTCTCAGAGTCTTTATGCGGCAA
CCAGCAGGGTCTGGAGGGTGGTGGCTCTGTGAACCTCTCTGACAGAACA
CAGAGATGTCTTTGGTCTGTGTGATTACAAGCTGAACGAAGGAAGA
TCAAAGCCAGTGACAGGAAGGAGATATGCAAGGGACCCGAGCATCAGCT
CTGAGTTAGTCCATTCTGCTTCTGGGACTTGGGATACAGGTCAGAAACCT
TGAGCTTCTACTTCTCCATCTTCCAATTGTAGCATCCAGGACCTCAGAAT
CTGCCAGCTAAGAGGAGCCCTAATGATTGTCTGGTGGGATATGGTGGGAC
CACAGAGATGAAGACATGAATAGCTATTTGAATGTGAACAGCAGACGAAG
AAATCAAGGCTAGGAGGGTGGAAAGTGAATCATCCAATAGCACAGTGTGGT
TGAAGCAGCACTAGTATCCAGGTTGCATGAGCCCCCTGATGCTTTCGCTCG
AGGGAAATTTTGGAGCCATGGGGCAATGCCCCCTGACGTAACAGTCTCCA
CAGTTCTGCCATGTCTCATCCTGGCCCTGTAACTGGACCCAAATCTGCT
ACCATCCCATCCATCTCAGGAAGTGAACCTCTTATGTCAAATAGGTTGT
GCAACGTATGTATCAGATCCTGTCTTCCCAAGGAGACCGCTCAGGCCACA
GCACTTCTTCCGATCCCCAATGAGCAGAAAATATCTCGCTATAAACATA
GTTGGCACTAAGGGAGGGAGTGAAGAGTGATGATGATGTAGATGGTGTAT
GTAGCCCCAAGGAAGTGAACAAGCAGAGATGGGGAGCTGGAAATGCCAG
GATGCTCCAGCTTTTGGGAATTATTCAGCTCTTGAGTCACTAAAGCCTT
TCTCAGCTGCAAGTTCTCTTTACCCTGTCAGGTCATTCTTCCAAGACAG
GAGACTGACATTTATTCAAAGCAGCAAGTGCCCTGATACCATCTTGTGTC
TAATCATGGGCTTCGCAGCCAGTTATCAAGGTTGATCTCATCTCATTGGT
CTTCAATCATTTTGAACAAGAAGACAAGCAAAATAATCATGGGTAGTTC
TTATATTATTGTGTGTACATGCAGTGATGTCTGTTCTTTGTAGTGAGCTG
TTCCTTCTTGTTCACCTCTTGTCTTAGAACAGAACTAAGCAATCTGCCC
CCAACATTTTCCCAATTTCCCATCTCATTCTTGGCACTGGCTTCTTAAT
ATTTGTTCTTATGAGTCATTTTCTTGTATCATTTCCATGAGTCCCTCTGG
GATCTTAAAGTATGAAAAATGTTGTGTGTACCCACACCTGTCTTTGTGGA
TATTTCTCTCCTTTCCCTTCTGCTTCTGGGATTATTTGGGAATGGGCACT
ATGATTTTTATCATATCGCTTCCACTTCTTTATGGCATCATCTCCAATG
GGCTTCTTCTCCCTCTTGGATCCAGGTTCTCAGATTGGGGACATGCAGAG
TCCAAGGAACATTCCATTCTCCTCCCTGGTCTAGAACAAGGAGGGCTTAG
ATATATGAGCAGGTGGCTGGGGCTGGCGAGCTATGTAGTCTCCAATGGCT
TTTCCCTGATGTGCGAGTTGTTATGTGAGTCTGGGAGACCAATAAGACC
TTGTCTTCTTCTTGGATCCATCAGAAAAAGCCCCCTGGGTGGGTAAAGATGG
ATGGCAGGGCTCTCCTACTCTATGTCTTTTCTCACACCTAGTGGGTATAA
GAGAGGGGACCACAAACAGAGGGGGCTCTGGTACCACTTATCCAGGGTCT
GGAAACATTTTCTGTAAAGGGCCAGATAATAAATGTTTCAGGTACAACCTA
CTCAACCTTGCATCATTTTCAAGAAAGCAGTCAGATAATACATAAATGAAT
GGGTGTGGCTGGACTTGTCTGCGGTCCCCTGTCTTATATCATTGTATTA
TATCATTTTTTCTTACATACAAATTTAGAAGCAATACTTAAAAA
GCCGTCCTTTATTGAGCACCTACTAAGTGCCAGGTACCTTTTTTCCCTC
ATTATCTTATTAACCTTTCATAATAACCTTTAAAGTAGATAATATTGAAC
CATTTGACCTATGCAGAACTGAGGTTGAGACAATAAATTATTTAAGACC
GCACAAACAGTAAATGCTGGAACACGACTCAAATATGGGTTAACTGAAC
CAAAACCAGATCTTTATTTCTCACTTTTAATTGTTACATATGTTTATTGC
CTCATCTCCTGTCCACATGGTGCCCATCGGCAGACTCCTTTCTCATTCTC
AGTGATTGAGTGACATTCTAAACTACATTGGCCTGGCAGATTACCTCTG
TCCCCTAAATGTTTCCACATTGTCTTTTAGGATTGAGATCCTCTCTGTT
CCCTTGCTCTTCCCTCCTTTCTTCTTCTGGCGGTGACGTGCTGTGTGAATT
TGTTTCTTTCTCCTCTCAGGGTAGTACTGGGACTTCCAAATCAGGGTTT
TTAGTGATCTCTCTTCCCTTTCTGAGTTTCTTCTTATTCCCATTCACT
TTCTCATCTATAAGTGGCAGCTTTGTTGCTGGAGGATTTCCTTTGTCTT
TTATTCTTCTTTAAGACTTTGTCTAACTGTCAAAAGCAATCCCTTGAAG
GTATCTGTCTTGGAAATTGTGTGCTTATGATGCTGAAAAATACTCTCTTC
CTAAAGCTATTATAAATGCT

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GGCTAGCTGCAACTCTTGAATACAAACACATTTCAGACATGCACACACTTT
CTGGCTCCCAAAAAGAAAAAATCAATTTATAATAATTCTGATCCT
TTGCTTATTTCCACAACTCCATGAAAATTGTACATTGTCCAAGCAACAT

TTCTTAATATTCTCTT...TCTCTCATATCCATTTTCCTTACTGCTGTC...
CACCTATCTCTTCCAACTCCCTGTTAAAATCCCTGCCCCAGCGAACTTT
TATTCAATTTTGTGGAATGGAGGCTGCACTGATTTAAATTAAAAA
AAAAAATCCCTACTCCATGTCCCAGATCCCTAGTTGTTTTTGT
TTTTCTGAGACAGGGTCTTGTGTCTTCCATGCTGGAGTGCAGTGGCATG
ATCATGGCTCACTGCAGCCTCAACCTCCTGGGCTCAAGTAATTCTCTTGC
CTCAGCCTCCCCAGTAGCTGGGAGTTCAGGTATGTGCTACCATGCCTAGC
TAATTTTTTCTTTTATTTTGTAGAGACACGGTCTTGCCAGGTTGCCAG
GCTGGTCTAGAACCCCTGGGCGGACGTGATCCGCCTGCCTCGGCCTCCCA
AAGTGCTGGGATTACAGGCGTGAGCCACTGCTCCCGCCTTGGGTGCAA
TTTGAGCTTTCTCACTTATTAGTGTAAGACATACAGCTAATTTCTAAATC
TTCCAAACCTCAGATTTTTCATCCATGAAGTGAGGATTATTATAGAGCTC
ACTAATAACATGGCTTCAAAAATATATAATGCCAAAATTGAGATCAAAAT
AATAAATCTATATTACATGGGAGATCTTAATGTACCTCTTATATTATGA
TAGACTAAGATGATCAAAAAATAGAAAGAGAGCAGTAAGGAGAGCAAGC
ATTTAATCAATAGGACCAATACATTTTAATCAATAGGATCCTCAGGAATA
TATACAGAATAACAAACCTAACAACCTGCAGAAAACATGCCAAACATTTAG
GTACAGACATTGTTGGAAAATGCAATCTTGAAACGAGTGGACTGACATTC
AGAAGATATTAATAAGAGCACTAATGATGGGGATTGCAACCATGTCTTTA
CTGACTTCCAGAAGCTTCTTACAGTAAACATGAAATCACATAATTTCTTC
CACTTTCCTACTGTTTCTTGTCTGGGCTCTGTCTGCTTACTGTCTAAT
ATCTTGGCCCCCTTAAAAGTTGCTAATCTTCCAAACCTCATTCTGTGACT
GGGCCGCTGGTCTTGTTCATGGGCCTTGAAAATACTGACTGTACACTTA
TCTGGAGCATCCAGTGCCTACCACCTGACCCAGATTCTCATTGCGCTCC
TCCCTCCTCCACCTATTGGAATTTGCTCATACCCGTGTGAGACCCCTCCC
TTTCCCCCATCTGAATTTTATCAAGACAACGCACTGCCATACTCCCTC
GTACCTGCTCTGGGCATCAGACTGAATGTTTGTTCATTGAGGATCTG
CAGCTGCATCAGTTTCCCCAGCACCGTCCAACCCCTGAGCATGGCTAGT
CCTAAAGCAGAGAATTAGCCTTTCTATCCCTGCTGCTATACATGCTGGGA
CAAATAATAAGAAATGACAGCATTTTATGATAATGCAGGCTGCAGGAGGC
AGGAGGCAGGAATCAAATTCGTGCTTATCAAATAGTGCTCCAATTCCTTG
AATATTGGACTATAGAATATGTCATGGATCTATGCTCAGGTGGGTCCCT
ATTACTCACTCCACTGAGGCCAGGTTGTGGGATTAGCTGTCCAAGAGGGA
GTTTCAGTCTCACAGCATAGGGTCATTCTGAGAATTACTGGCCCACTT
GTGTGGAGACCTCCAGAGAACAGAACTCTGGGTTGGTGCCATGTACTTCCA
GGAGGACAGATGTTGGCAGGATGCCAGCCCCACAATCAGAGGGGAAGGGG
CAGAGCCACATGTATGAAGATCCTCTCCCCAGTACGTGCCAATCACAGGG
CTTCTAGCTTTTGGGCCAAGGAAACAATGTGGGAAGCAAAAAAGGACAA
TTTTCTCTCCCTTTCATGAAGACTGAGCAGTTTACCAGATTCCCAGG
GAAACACCCCTTCCACTCTGGGTTGAATGTGAGTGAGAGACATTCAGCTGG
AACACTAGAAAACTATTTCTGAGCCACTCACCTTTAGCCCTAGAAAGT
GTTGGATTTGTCTTTCATCTTTGCCACAGTAGAGACTGCTGATAGCATCA
GAACCTTGGGCTCTGGAATTAGACAGATATGGGTACAAATCTGAGCTCTCT
CACTTATTAGTGTGGGATGTAGAGCACTTTTAAATCCTTCCAAACCTC
AGACTTCTCATGCATGATGTGAGGATTGTAATAGGGCCCACCTAATAGGG
GTTTTTGAGAAATAAAAAAGTTATTCAATGAACAGCATTTAGCAAGATGC
CTGACCATTGAGAAAATAACAAATTGTTTATTATTATTGTTATTATTAA
CATCTTCTGACCTTCTGACTGGGGCATCGTATCATCAGAAAATACTT
AGGATGGGATGGATTCTGTCATGGGCTGAGTCAAGGGTGCAATAATGGAG
GAGTGAAGAAGGAAGAAATGGAGGCAGAAATCCCCAGGAGCCCAGCATGG
TACAAGGCTGAGCTAGTGTGTCAGAGCCTCCTTGGAAACAGCCACAGAGCT
TGCTCTGGCCCTGGGAGGAACCTCTTCTAGCTGGCAGGACCAGCCACAA
CAGTGGCCAGGGGATTTCCAGGGCGTGGGCTCCTAGGAGTTTCAATTTGGA
CCAAGCCTGCCTGGAGAGGGGTATAACAGGGATCCTTCCCTACTGGCAG
GTGATTTACCCCTCGGTGAGAAGCTCAGGCATTTGTTTGATGGAAGGTGG
AAGGCCCTGTGCTGGGCCAGTGACTATCAGGGATGGGCGGGTGGCTGGAA
AATAGCAATAAGACAATATGATAACACAGTTAACCACCACACTATGTGA
AGCTACAATATGGGTATCTGTAATAGACAATTCCAATGTAGAGAATAATT
CTAAGGTGTATCTCTCCCGCCAATGCCATAAGCACACGGCCTCTGCCTG
GGTTTCTCACTGTGGAATGTCCTCCTGGTCTCCTCATGCCAGAGAGTGG

FIG. 3 (46 of 52)

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GAAGTACTCCTACTTT. .CACCGGCTTTCCTGTCATCTCCCTGCAGCC
CCTCAGCCCCCTCTGCACAGGGAGGTTTCTCCCTGCTGCTGCAGTGCTT
TGTACTTGTGTAGTGGTACCTGCACACAGGTATTGGTGTCTTGTCTCACC
ACCTACATCACTGTAAGCTCCCCAGGAGCAGGCTTCTGTTTGACTCAC
CTGTGATCCTCCACCTCCACCTGTAGTGCTTCAAGCATTGAGGACAAT
CACTGGCTGCCCTTAACCCAGAAATGCTGCCGAGACAGGAGGCCATGGC
CCAAGTTCTGGAATGGGGTATTACTATGTCAGCACAAAGGCCTTTGCAC
AAATGAAGGCTTTAAAAATGCAGTCTTAGTCAGGTGGAGGAGGGCTTATA
GGATTCCCAGGAATCTGGATCATTCTCTTGAGAGCTTTCCCTTGTCTCTG
TTAAAACTCACATCCTACGGCCCCAAATAACAACAAAAAATGGATGTAAAT
TCTTGAATAACTTGTGGATGGGGGAACAAGGCCACCCCCCAGATCTGC
CAGAAGCTTCAGGTGAGGGTCCCAAATGCCAAAAAGTCTGGTATCAGAGA
GGATGGCCAGTGACCTGGGGACACATGCCCTTTGCTGTGTCACTCAAGGA
GCAGCAGCCTGGCCCCGCACAGTGACCAGGACCCTGGCTTCCCACGCTG
GGCAGGAGCTGGTGTCTGATGAAGGGAATGCCTGGCAGCACGTGCTGTCT
GTCTCCTCGTGTGAGCTTACCTGGCTTTGCTGCGAAGAGGCCACTCGCAT
TTCTCAATTTTTTATATTTTTTTAAATTTTTTAAATTTTTTATTTTT
TATTTTTATTTATTTATTTATTTTTTAATTTTTTTTTTAATTTTTTAAATTA
TGCTTTAAGTTTTAGGGTACATGTGCACATTGTGCAGGTAGTTACATAC
GCATACATGCGCCATGCTGGTGCCTGCACCCACTAACTCGTCATCTAGC
ATTAGGTATATCTCCAGTGCTATCCCTCCCCCTCCCCCACCACCAA
CAGTCCCCAGAATGTGATGTTCCCTTCTGTGTCCATGTGATCTCATTG
AATTTCTTTAAAGGTGGAATCTCTCAGTGGGGTCTAATCTGTTCAAGAAAT
ATCAAAAGAGTATCCTTGGAATGACTGGAATTCCAGAGTCATCTGGTAA
TCCTCATAAAACAACCTCTGGATGTCTCTCAGCACATCTCCACCTTGAA
CGCAGGAGCTGGTTCAAATGGAGGAGCATCGCTCTACTGCATTTTTTTT
TTTTTTTGGCCTAAAGTGCAAAGGGGATACGTTTCATGTAAATAAATCA
ACTGCAAATCGCTAGTTATGCTGAGCCCTGTCCCGTGTGTGGACACAAA
GGAACCAAAGGCTTTTCTCCCCGCCCAACACACACATAACACACACACAA
AATCATAAAAACATACATACCCCCAACACATAACAACACACAACACACAC
ACAAAATATATACACACAACACACACCAAACATGCCCAAAACCTGTGTC
CAGAGATAGATCCTACTGGTGGGTTTGTGGTCTCGCTGACTTCAAGAATG
AAGCCGTGGACCTTCGCAGTGAGTGTTACAGCTCTTAAAGATGGCATGGA
TCCAAAGAGTGAGCAGTAGCAACGTTTACTGTGAAGAGCAAAGGACAAA
GCTTCCACAACCCAGAAGGGGACCCAGCAGGGTTGCTGGTTGGGGTGGC
CAGCTTTTACTCTTTTGGCCCCCTCCCATGTTCTGTTTCCATCCTATCA
GAGTGCCCTTTTTTCAATCCTCCCTGTGATTGGCTACTTTTAGAATCCTG
CTGATTGGTGCATTTTACAGAGTGCTGATTGGTGCCTTTTACAATCCCCCT
TGTAAGACAGAAAAGTTCTTGATTGGTGTGTTTTACAATCCTCTTGTAAG
ACAGAAAAGTTCCCCAAGTCCCCACTGGACCCAGGAAGTCCACGTGGCCT
CACCTTTCAACTCCATAATGGCATGAAAATACATATGTTGTACAAAACAT
ACATACACAAAGTATACATGCATCTCCCCAAATATACACATACCACAGAA
ACATACACACAGGAATCAGCTACCTGTCAAAGTCTGCATGGTGAATGTC
CTCTGCAGTGAGTAGTTAGAAAAGTGAATTTGTTTTTCAATAAATTGGAG
TCCTTAAAAATCGTTGTAAGATAGAAAATTTTTTAAAGTATATAAAATAA
AATATGTATGTCCTTTGGTCTAGCATTACACATGTAGGAATTTATCCTA
GTGGAGTAATCAATGATATATGCAAAGATTTGGACAAGCATATTAAGCAC
AGAATTATGTATGCATATGTGTGTGTATATATATATATATCTCATAcata
TAATAATGTAAAAGTGAAAATAACTCAGATGTTCAAATTTGAGGATTAGT
TAGACTATGATCTGTCCATATGTGACATACAAGTTAGCTGCCCTTATTC
TCTCGAGCTTCAACCTCCTATAAACAGTGTCCCTGTATATCAGTATTGG
TACAGATAATCGAACTTATTGAGGTTTTACATGGGGCAATAAAGGCAAGA
GTTTATGAATACTCCATACTACACTAGGTAGCACCCCCCTATTAAAGACAA
ACTCTTCTCTCTCATTTCCTTCCCTTCCGGAACCACTTGGTTGAATCTC
TACAAGTCTCTATTGCAACTGCCTCAACATGGCACCCCTCCCTGCATCTCC
ATCTTCCCTGCTCTGAGAGCAATGGCCTGCTGCCCCACACTCACATCCT
CATTCAATCCAGAAGTGAGCACCACAGAAGTGCTACAGTTACCCCAACC
ACCTTCTTAGAAGATAAGTTAGTGTGTTTTGTTTTGACTTTTTTAAATTTTTA
CTTCTCTTTTCTTCACAATCTCATCCCATCCCAAGAGGTTTTATCAAGA
AGTTCTCTAAAGATATGTGTCTCCTTATGGAATTTAACAGAAATCAGGGA

FIG. 3 (47 of 52)

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TTGTAATCTAGCAAT AGGGAATAACATTTTTCCAGGTCTTTAGAC
ATAATGGAATACCTTGAGTAATTAGATACACTATTGTAGAAAAGTATTG
ATGAAATGGAACGATGTTTGAGATATCATATTGAGTAGAAAAGGCAAGAT
ACATTAAAGTAGGAAATGTATCTTACAAAATAATTTGTCAGACACACTCCT
ATATTTGTATGTTATATAAATGCGTATGTGAAGAAAGGCTAGAGGATGAG
ACCACAGTCTTCGGTGAAGTTTAAAGAGATGATGCTGCAGCATGCTCAGAA
AGGCTTGGTATAGTTTTTCCAGTAATTAAGGACTGATCTTAGGTAAATT
GTCATCCTCTCTAAACTGCACCACCTTTTGTCTGTAAAACAGGAAGGAT
GGTATTTACCCCGAGGTCATCAAAGGATTTGGTTGGAGAAAAATAAATA
AATGGGCTGAGCCCGAGACCTGGCACAGTGAGAGCACAGTGGTTGACTATT
GTGCTGGCCTGTTGTTCTGTGTTATTGACATGCTGCTGGTGGTGGTCCA
GAAGCTATTACCTTAATTGGTTATGTGGATTTCCCCTCATACTGAGCAGC
TGTGTGTGGTGTGTGTAACATAGCCATACACAGTAAGTACAAGGGCAA
ATGTGATGGAATAATGCAAGGAAGTGCAGATAAATAGCTAATGGGCTGTA
GAAGGAAGCTAGTCCTTGGAGGGCTTGATCAAGGAAGGTCCTTTTGCATG
TCACCTTTGAAGAAGAGGGGACATAGAAGAGGTATAGTGCATCCCGGAGT
GTACCTGGAAGGGAACATGAAAAGAGGACATTTTCTCTGGGACATGGGG
ACTCCACTTGCATGAAGTCTGGAATTGGGGCAAAGAACCATCATGAGAAC
AAGGGCTTCCCTGAACCTCCAGGCTCATTGGCTGATCTAAACCTGTGT
CCCCCTTTCTCTACTCTCTCTCTGTTTTCTATACCTGTATTATTGGACT
GGACTGGAAGCCACCTGATCTATCACAAGTACCTTGAATGTGTTGAATA
GGTGTGGCACAGTCTTAGCAGAGTGGCACTACCCCAACAGGAATTTGTT
TATACCTTTGGCATGGAATAATAGCAGGAATGAGTGATCACTGATAACTG
AGGATGCTATTATTATTGGCCAAAGGAATACTTGTGTTGTATTTCATA
ACCACTCACAACTGTTGATTACAAATGAGTACCAGACCTAGCTCCTTCA
AGTAAAGGATCTTGAGAACTGAAGGCAAACAGAGCTCCAGGAGTCCAAGA
CAGAGCCACAGACCACGAGGATCCCTGGCCCAGGTAGGTGGTCCCTCCTGC
ACTGGCTTTCAAGGCCAACAGGATGGATGGGGAAGTAGAGTAGCATCTGG
CCATCTAGACCCTTGCTTTTTATCCCCACTGGAAGCACATCTGAATTTCT
AAATATGATCTCTGAGACCTGCCCAGAACACCTTGCTCTCAGCCCCAGTA
GCAGCCTGCTCTCTCCAGGAGGGCTTCCACTAACAGTAGGGCATTGCT
GGAGGGCCAGGCAGACACTAGCTTAGGAAATCCACCAACCTGGAAATGC
TAGTCCCTTCTCTGAAGGCTCAGAAGACTGACTTTAGAGTCTAGAAAATA
TTGGTCTTGGGAACAGATTTTGAAGTGCAAAGAGATGGACTTCAGATGGC
CAGATGCACTGCTTCTTAGGGAATTCTGTGAAAGCTCCCTGCATTTATC
TTAATACAGGCAGCAGATTTTATGAGTACCCCGAGGGATGGCCCCAGGT
CCTCCAGCCTGTGAGCATCCTTCTGTCTTCCAGCAGCACCACAGTATCTT
TATATGCTTTGGATACCTACGTTTTCTGCCAGACATCTCTTGCTCTGATG
TTCTGGCTGCCAAATTCTCTGTCAAGCGCCTCCAATTTTTTGTGTCCTTT
GATTTACCCCAACATGACAAAGGCAGTTGTGCTTCATGTATTCAGGGATA
CTGCCAAACCAACAGGTTAAATCAAATAGCAGATATCCCTGTTCTCCT
AAAGACCCATCAGCTCTACCCACCTGCTCCTGCTCACCGTCTTATTGTT
GAGTCTTGAAGCCCTTCTTGTCAATTTTTATTTTTTGCATGAACAATTTA
GTTCCCTTGTCTCACTCCTAAACCTTTCTCAAAGGATTGGATTGTACA
CAAAGTGCCTATCTCTGCAATCTTAGAAGTGATATGATTCTGAACAAATC
ACTTAACTTTTGAATTTTTATTGGTAAGATGGGAATACCAATTTTTGCTC
CACTTCTGTCTATGTTGGCCTGGGCTGATGTTGAAAGCTCTCGGTCAAC
TGAGATAGGGTGTGCAGAAATTTATATATATAAATATATCTCCTCCAACCC
CTCCCAATGAAGCAAGTCACGTGAGTCAATCCTACCCTAAGATATTAGGG
ATTGAGCCTCCTGGGACATTTGGTGGCTTAGGTTTTCATGAAAAGAGGTT
GCAGAGCAACTGCTTTTTGTTAGGCAAAGATTAGGCTACTGCAGAGACTC
AGCAAACCTCTATAGAAGGTGTCAGATGGTAAGTATTTTAGGCTTTGCTT
GCCAGATGATCTCTCAACTAGTTAACCATGCTATTGTAGCCTCGAAGCAG
CCAGAGACGATCTGTAAACAAGAGCATGTAGTGTGGCATAAATATAGTA
CCGCG

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GCAATAAGTCTATTTACTGTAAAGTTAATCAAATTTACATTTCAGAACAC
TTAATCTGCAAGAGTCCTTTCCAAGACCTATACCTAATTTTGTGTTTAC
AATTTTATATTTGTTTTCTTAAAGAAGACCACCAATATAAACTATATCCA
GCCTTCATGATAAGTACATAAGAACTATGCAAATAAGGGGGAAAAAAA

FIG. 3 (48 of 52)

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CAAAGAAAAATACCTAC CTACTAATGGTTCACTTCTGAATAGCACAT...
TCATAATGATACAAGCACTCATTACTAGTCTAGGAAAATGAAGATATAAT
TGCATTAGGAAGATCAAGAGGTAGGAAATGTGGATGTGTGTGGTATAGAC
TAGGGCAGGACAAAGAACCCTAAATCCTCATTCTTCTAAAGATAATTGTAA
TACGTAAAACCTCAAAATTCAAGAAGTAACAGTAAAAGCGGTCATTAAGAA
ACAAGCACTAAACACCAGATAGGAAGCGAGAGATGGGGGAAGAGGGCAAG
AATCTGATTATTTTTTGTCAACAAATTTTGTAAAACCATTTGACTGTTTAC
ATGTAGAACTTGGATCTTTTTTAAAAAACACAAAATAATAACTATTAT
TTTTTAACTGGATTTTTTGA AAAAGAAGATAAAAGTCTCATTTTAGTAATT
AAAACCTCATTCCAGGTTAGTCCACTCAAACTTATATTCGAAAATTAAAA
CTTTGGGAGGCTGAGGCAGGCAGATCACCTGAGGTTGGGAGTTCCGAGACC
AGCCTGACCAACACGGAGAAACCCCGTCTCTACTAAAAATACAAAATTAG
CTGGGCGTTGTGCATGCCTGTAATCCAGCTACTCGGGAGGCTGAGGCAG
GAGAATTGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAGCCGAGATCACA
CCATTGCCTCCAGCCTGGGCAACAAGAGTGAACTCCATCTCAAAAAAA
AAAAAATAAATAAATAAATTAACCTCTGGAAGTTGAGTTGCAGATATTCAT
TATGCTCATTTTTTAACTTGTATGTTTGGAAAATGTCATGATGAGAATTGA
GGTTGGGGGATGAGAAAAAAGAAAAACATCAACCCACAGCCCATTCAA
TTTTTCAGCCCGACCCACAGCTCCGGGGAAGGGCAGCAGGTCCATCCTTCA
CTCTTTCTTCACCTCTTCCCTCCTTCTGGCTCTTCCACCTCTAAGTTG
GAGCCCAAGAAGAGGCACTGGGAAATGGAAAAGTCTTTTGTACGTGGTAC
TTGCCGGGGAAGCTGCCATGAAGACCTGGCCCCACGGTGGGGAGGGAATG
CCCAGCTGAGGCCTCGTGCCCATGCTAGGATAGACTCGTCCAGACATGTC
AGGTGGTCTGCAGGGCAAGCAGCAGGAAGTCATGTATGAGTATGAACTG
ATCTGTATGCAAGGGCGGGGAGAACACGCGGAGGAATGGGGCGTGAGAAA
ACAGCACAGTACGTTTCTTTAGCAGCTGTCTCTGCTCAGCCATGGGAGTC
ACCAGAGAAAGAGGCTTGGAGGCGTTATTTTCACTGTGAGATGTGAGTGT
AAAAAAGTGCCCAAGACACAGTGAGTACCAGGGAGATGCCCTCTTCCCT
ACCCGAATGCAGAATGGCCACAGGCCTTAAAACACACACATGGTTCCTCA
GAGGAGAGAGGCCTCCACAGTGGACACCCGCATTCTCCCTGGTCAGCAG
CAGCAGGGCGAGTGCTGGGCCATCATGAAGCTTCACAGGCAATGAGCTCT
CAGCAATAACAGGAACAGTGCCTGGGGGACTGTAGCTGCAAGACCGATTT
TCATGTAAGATGGCCTCTGAGGACTCCGAGATACACCAGGCTGAGACTAG
CTGGCAGCTCCAAGTTCTTGGTCAGAAGAGAACAGGAAGTAGGGAAATTG
GAATTACTTACTACAATTCTTTACATCCGCACAACCATGAGGTCCAG
AGAGTCTCTCTTATTTTTTTTTTAAAGACAGGGTCTCACTCTGTCGCCCA
GCCTAGAGTGCCTGGTGTGATCATGGTTCAGTACAGTCTTACCTCCCA
GGCTCAAGTGACCCTCCTGCCTCAGCCTCTCAAGTGGCTGGGACAGCAGT
TGCATGCTACCAGGCCTGGCTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT
TCGGTAGAGACTGGGTCTCTCTGTATTGCCAGGCTAGTCTCGAACTCCT
GGGCTCAAGTGATCCTCTGGCCTCAGCCTCCCAAAGTGTTGGAATTACAG
GCATGAGACACTGCACCCAGCCAGTATAGTCTTTTAAACAGCTTTATTGAG
GTACGGCTAACATTGAAAAAACTACACAAATGTAAAGTATGCAATTGAT
AATTTTGACAAATGTACACACCAGTGAACTATCACTACAGTCAAAATAA
TGAACATATCCATCACTCCCAATTTCTCAGCCCCCTTGGTAACCCCTCT
CTCCCAACTCCCTGCCCCCTAACATCAGACAACTACTGATGCATTCTGTC
TCCATAGGCTCATTTACATTTTCTAGAATTTTACATAAATAAAATGACAG
AGTATATACTCCTTCATGTATGGCTTCTTTCAGCCCAATTATGTCAAGAT
TCATGCTTATGGCTGTGCGTATCCTTAGCCCATCTCTTGTCTTGCTGAG
TAGGATACCATTGCATAGACAGACCACAGCTTGCTCATCCATCACTCTT
GACAACGTTGAATTGTCTCTGTTTTTGAATGACAAATAAGGTTGCTAT
GTACATTCTGTATAGACATTTGTAAAAGCACAGCATTTTCATTCTCTTG
GGTAAAGACCTAAAAGTGGAAGGCTGAGTCATATGGTAAATATATATGT
CTAACTTTTTAAGAACTGTCAAAGTGTACCCAAAGGGATTGTACAATT
TTACATATCCCAAGCAGTGTATGAAAATTCCCGTACTTCCACATCCTCA
CCAATATATGTTGGTCAATCTTTTTTAATTTTGGACATGNTAATGAGTG
CAAAATGAGGCCAGAGTGTCTGAAGTTACATTTGTATCCTTTTGGCAT
CCAAAACAGGTGTCAAGCATAGAAAAAACACTTGTTCTTGAATGGTCAG
TCATTTACAAGTGGAATTCATTACAAACCGGTAGTTCTACTGGGTAAAC
TATGCCTTACTGTCAACAGGCACATACACATACAGACAGACAGGAAGGCA

FIG. 3 (49 of 52)

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CAGAGACAAGGCAGAGC...TGATAAGAAGGTGACCTGGGCTCTAGCTCT
GCCTATCACCTAGTAAAAATATTAGTTAAGTAGCCATGAGTAACTCACTTA
ACTTACCACAGGCTCCATTTTCTTATCTGTAAAATAGGAACATTGAAACA
GCTAATCCCCAAGGTTTGTGGATAATCAGAATTACAAAGATCAATGACAT
TTCTATGAGAGAAACATATTTCCAAGTATTTGATGGAGTACATCAGACAC
AAAGGAAAGGAACTGAATATTTTGGAGTTTTTTTTTTTTTACCAAGAAA
TTCACATTTTGTAAATTTTCAGAACTACCTCCTGAGGAAAGTGTAGCTG
CA⁵CCATTTAGAATGATAGAAAACATCAATCTGTCTGATTCCAAAGCCAA
GTTCTTGCTACAACGAGAAATGAAACAACCTGGATCCCTACAGATGCAGAG
ACCTGGGCCCCACAAATGTGAATTCTGTTCCCCTACCGAATAGAGTTACA
GTTCCATAATACAGTACTCCCTCACTTTTCCACAGTCTCACATTCCACAG
TTTCAGTTATCCCAAGTCAACTGCAATCCAAAAATATTAATGAAAAATTC
CAAAAAATAACAATTGAGAAGTTTTAAATTGTGCTCCATTCTGAGTAGCG
TGATAAAATCTTGTGCCACCATCCACCTGTCCAGCTTATCGTTAGTCAT
TGACATCGTCTGCTCCTGACATCCAACCATTGACATCATCATGACTCTAT
GATCCAGGATCACCGAAGCAGATGACCCTCCTTCTGACATATCATCAGGC
CAATATCAGCCTAAACACTGCATCACTATGCCACATCAGTCACCTCACT
TCATCTCATCAAGGAGGCAATGGATCACCTCACATCATCACAAGAAGAAG
AGTGGGTATAGAACAATAAGATAATTTTGGGGCAGGCATGGTGGCTCACG
CTTGTAATCCCAATACTTTGGGAGGCCAAGGCAGGAGGATCCCTTGGGCC
CAGGCATTCAAACCAGCCTGGGAAACATAGTGAGACCTCCTCTCTCTGC
AAAAAAATAAACAATAATTTATCCAGATACAGTGGTGCATGCCTGTGGTC
CCAGCTACTCAGGAGGCTAAAGTGGGAGGATCACTTGGTCCCAGGAGGTC
GAGGCAGCAGTAAGCTGTGATCGTGCCACTGCACTCCAGCCTGGGCAATA
AAGTGAGACCCTGTCTCAAAAAAAAAAGGTAATTTTGAGAAAGAGACCAC
ATTACATACACTTTTATTATAGTATATTGTTAGAATTGTTCTATTTTATT
ACTTATTGTTGTTAATTTCTTTCTTGCCTAATTTTTTTTTTTTTTTTG
AGTCCGAGTTTCACTCTTGTGCCCAGGCTGTAGTGCAATGAGACGATCT
CAGCTCACCGCAAATCCCGCCTCCCGGGTTCAAGTGATTCTCCTGCCTCA
GCCTCCCGAGTAGCTGGGATTACAGGCGCCTGCCACCATGCCAGCTAAT
TTTGTAATTTTAGTAGAGGCGGGGTTTCTCCATGTTGGTCAGGCTGGTCT
CGAACTCCTGACCTCAGGTGAGGCCTCAGCCTCCTAAAGTGCTGGGATTA
CAGGCTTGAGCCACTGCGCCTGGCCTCTTGCCTAATTTATAAATTAAAC
ATTGTCACAGGCATGTTAATTTATAGGAAAATCATAGACATATAGAGT
TGGGTACTATCCACAGTTTTCAGGCATTCACTGAGGGGCTTGGAACACGCC
CTCCTCAGATGAGGGGGGACTACTGTCTCTCCTCAATCATTCTTGATT
AATCCTCAACACAAATGGTTTGGCCAGGTCTTGCTCTGGAGACAAAATT
GCTAAGGATTTAGAGGGGAAAAAATGTAGTTCACTGGGAAAGTCACCTCT
GCTCCACTGGACAGCAACTTAAACCCAGGCCATGACAAGTAGAAAGGCC
ACCCCACTCTCCTTCACACCTGGAGTATTCAGGAGTCAATCATATTTCA
GGACCACCAGGAGCAAACTGGGAAAACTGAGCTGCCTTGAGGAAAGCAA
TCAGCTCCACAAGGGGCTTAAGAAACAAGCTCTGGGAGGAGTGGTTGGAG
AAGAGTTGGGGACACATCAGAAATGCCATCAAATTTCTAAGGGCTACCTC
GTGGTGTACAGCCTGTGCATCTTCAAGGACATAAACAGATGGGATAAGCA
GATGAGATTACAGAGGACATCAAAATATTGGCTCCCCAGAAGGGAGAAC
ATTCTAGTAACAGAGCTGCCCAGCTGCAGAGTGGACTGTTTCACAAAGCA
ACAGGTGCCCTGCCTCTTGAATCACCATCTTCACAGGAATGCAGTAGAAG
GGACTTAACCTCTGCCCTGAAGAAAAGGTTAGGCTAGGGAAACAGCTCCA
AAATTTTTTAAAGGAAGCAACATAGGCATCTACTGGGAGTTTTCTAAAG
CCTTTGTTTAAATGAACTAAAGAGCTGGGACAGGAAATGCCAAATTAAAT
TAATAGAGCCTTGCTTTAAGACAATGCAAGTGGATGGTAATGAAGGAATG
AGTCTTAGGCCTTGATCAACCGTATTAAGCAATGCTGAGCATGGAGCCA
ATTCTGTTCACTAGATTTGCTCAGAAAGGGCCAGACGAGAAGGATTTTTC
TAAAGGCCACTACTACCAAAAAGCTGCCAAGCGTCCAATGGAGCCCAGA
GAGAAATATGCTAAACAATAAAAAGTTGAACACCCCTCAATAAAAAAGGGTAA
AAGTAATTAATAGAAAATTACTGAAAGCTTTTTTGAAACCAAAAGTAGTC
AGCATTGGTAAAAGTCTACAAAAGTGGACACTTTTCATATAATGTTGGCAG
GAGGGTAAAAAGACATAACCTTTTTGGAGGACAATTTGGCAACAGAGTAC
CAAAAACCTTACAATTGAAGAGAACTTTGGCCTGAGTGCAGTGGCTCACA
CCTGTAATGCCAACACTTTGGAAGGCCAAGGTGGGAGGATTGCTTGAGCC

FIG. 3 (50 of 52)

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CAAAAGTTTGAGACCAGCCTGGGGTAACACAGTAAGACCTCGTCTCTATG
AAAAATAAGAAAAGTTAGCTGGGCATGGTGGCATGTGCCTGTGGTCCCAA
CTACTTGAGAGACTGAGGCAGGAGGATCGCTTGAGCCTCGGAGGTCAAGG
CTGCTGTGAGCCATGTTTCATGCGACTGTTCTCCAGTCTGGGTGACAGAAT
GAGACCTGTCTCACCAGAAAAACAAGGCAAGAGAGAGAGAGAGAGAGAA
GGAGAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGATGGAAGGAAGGAAA
GAGAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAA
AAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGGAGAGAAAAGGA
AGGAAGGAAAAGAAAAGCAAGCAAGCAGGAAAAGGAAGGAAGGAAGGAA
GGAAGGAAGGAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAAAGAAA
GAAAGAAAAGAAAAGAGAAAAGAAAAGAAAAGAAAAGGAGAGGGAAGGGA
AGAAAAGGACAAAAGAAAAGACCTTTGAACCTGAATTTCACTTTTAGAGA
TTCATCTTAAGGAAATTCATTCCAATAGAAATTTATCCCCAGGATTATCT
AAATATTTGCTTTTATTTTCTTCTAGTAATTTTATGGTTTAACTTTCTCA
TGTTTAAAGCCTTTAATTTATTTGGAATTTATTTTGGTATGAGAAAGTGTG
ACCTTTTTTTGTTTTACTTTAAAAAAATGTATTACGATTATTATTTTAG
AGACAGGGTCTTGCTCTGTCAACCAGGCTAGAGTGCAGTGGTGTGATCAT
AGCTCACTGCAGCCTTGAACCTCCTGGCCTCAAGCAATTCTCCCTCTTCAA
CTTAGGAGTAGCTGGGACCACAGGCATGTACCACCATGCCCACTAATTT
TTTTTATTTTTTGTAGAGACAGAGTCTTGCTTGTTGCCAGTCTTGCAAT
GTTGTCTCAAACCTCCTGGGCTCAAGTGATCCTGTCGCCCCAGCCTCCCAA
AGCACTGGGATTACACGTGTGAGCCACTGCGCCCAGCTGCCTTTTTATTT
TTTAATTTTTTCAGATGCTTTGTTGGTTCCAAAATAGCACTTATTAACCCA
CGCTTTCCCTCTGGTTTTAAATACTGCAAGTTTGGCTTTGAAATACAA
CCCACTGCCTTATTCAGGCTACATTCAAGGAAATCTGAGACCAAGAGTCT
GAAGGCCAGTTTCTTCTCTCAAACCCAGGAGGTGGTAAATGTGTCATT
CCACCTTTCTATCTATTCTAAGAATCCTTCTTTCCAACTCTGACAT
GCCCTGGCTCAGGTCTATAGAAATTCAGGGTCCACAGACAAAGCAGA
ACTCACTTATGGGGAAATCTGGGAAATACTTATCTGTTAAACCTGCCCA
TATGGTGACTCAGATTGTCTAAAGCCCAAAGCATCATTTTCCACCCCAA
CCATTTCTCCTCCAGACTTCTCTATTTCTGTGGTCCAGAGTCAAGATCT
TGATATTACCCTAGAGTCCCCCTTCTGCTCTCCTGCATACCCAGATGCCC
CTCCCTCCCCAGATCCATTCTCCACCCCTCCCTCCCATCAGTTTGGTGGG
CCCATCACCGCTTCCCTGGCCCCAGGCTCTCCTTTTGTGCGCTTGGAGCA
GCAGACTGATCTCCAGCCTTCACTCACTTCATGTGGTAATCTGTTGTGT
TCATCACTGTGAGAATCTTCTGCATCCCCCTCACTACTCTGCTGAAAACAC
TCTAGTGGTTCCTCATTGCTCATTAAATGAAAGTCTAGATATTAAACGTAG
AAGGCCAGCACAATTTGCCCTATGCCACCTACCTCTAATCTTTTCT
CCTTACTCTGACAGACTCTCCGTCTGTCAATTTATGTATTCTTTTATTGCT
CTCTTCTACTTTTAGTATGAACTGGATTTATGGATTTTTTTAAACATTGCT
TTCAAGTATGGAATAAAGAATTTTATTTATTTATTTATTTATTTATTTGA
GACTGGGTCTCACTCTGTTGCCAGGCCAGAATGCAATGGTGCAGTCATA
TCTCACTGTAACCTCGAATTCCTAGGCTCAAGCCATCCTCCTGCCTCAGC
CTCCTAAGTAGCTATGACTACGGGTGTGCATCACCACATCTGGCTAATGG
AATAAAATATTACAATGCCTAATCTTAATTTTCAAAATTTTAAATTACAT
TGTACCTAATGCCCATGCATTTACTTTTTTCACTGGGTCAATAGCCCTCA
CTTTGGCAAAGTCCCAGGCCCAAGGTAAGGCCTTACTTTTTCCAACTC
ATCTTTTGAAAGACATAAGTGCCTGTAAGTTGTACCATTAGGTTCTAG
GAATTTTTTATCAAAGACTTTATCAGACTATTTTCTCTAAGTTGAGAAA
GAGCTGGGGGCAGAATATGGCACTGAATGACTGAAGAGAAGGCACTGAAA
TCAGGCCAGAGGTTGCTGGAAAGAGCAATGAGGAACACCAGCAGCAATGA
GGAGCCGGTGATGATTTTGGCTTCACAGGGAGGTGTGTACCACACCGATT
TTATCTCTACGTGGATGAACCACAGCTGTCGGCTCCCTTGTCTCCAGGAC
ATCACACTCTCCACATTCCTTCCCATCTTCCGGCTTCTGCTTCCCGGGGC
CCTCATCTGCCCCATCCTGGGTGAACACTGGTCCGTCAACTGCTGGGCGT
ACCTTCCCGCTCTGCACACCCTCCCTGGCCACCCCACTCTCACGGC
TCGCACTGCAGAGGAGCCGCATCTTAGCTCCAGCCCATCTGCCTCTTCT
GAGCTCTAACTCATGTAGGCGACTCCTGCCGGTGTTCCTCACAGGCC
ATCATACTTCAAAGCATTTTTCCCTCAGAACACCATGTCTGGCTGCTCC
CTCCAGAAGATACATCTCTCAAGCACATCCCCGCGCTCTCACCTGGATG

FIG. 3 (51 of 52)

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ACTGCATTACCTTCTC ACATTTGCCCTCCTTTGGATGTATATAGA.
GTTTTAAATACAAATCTGATGTGCTTGCTCTCCTGCTTGAAACACCTCA
AAACTGCCTTCAGGATAAAACCACTGCCCTTGACATGTTACAGGTTGCCC
ATGGCCTGGCCCTGCCCATCTCTTCAGCCTCATCTCATGCCCTTGCCCC
TCGCTCTCTGGGCTTCTGCCTCCCTAGCCCTCCTTTAGGTTCTCTAACAC
ACCATAGTCCTTCTAGTGTGGGGCCTCTGCAAGTGCTGTTCCCATTGCC
TGAGACATGAATCCCTCTCCCTATCTCTACCTGCACCTTCATCTGATTAA
TCCCTACCCTTCCTACTCATGATGTTGCTTTCTCAGGGACTCTCTCTGAC
TTTTTAACTAATCAGGGTCTCCCCAGTATATATCTTCATAGCACTCTGT
ATTACTCCTTTCTTAATGACCACCTGCTGTAGACTGAATGTTTGTCTTCC
TCCAAAATTCATATGTTAAACCTAGCCCCAAATGTGATAATATTTGGAG
GAAGCTCTTTGGGAGGCAGAGCCCTCATGAATGGGATTAGTAGCCTTAT
AAAAGAGACCCCTGAGGGCTCCCTTGTCCCTCCACCGTGAAGGATGCA
ACAAGAAAGTATGGTCTATGATCCAAAAAGCAGACCCCTGCCAGGTACCC
AATATGCTGGCACTTGAACTTCCAGCCTCCAGAACTGTGAGAAATAAAT
TTCTATTTTTTATAAGCCACCGAGTCTATGGTATTTTGTATAGGAGCAC
AAACAGACTGATGTGCCACCCAACCATGATTATACGTGTAATTTATGGTT
TCTCTGCTAGTAGGGATGCACCATGGGGTTAGGAACCACGCTTTTCTTAT
TTCCACACAGTCTTAGCTCTAAGCATGTTCCCTGAATCAAAGATCCCCA
TCTTTTATGAATGAAGGAGTCAGTGAATGAATTAATGAAAGAAGTATAA
CCCTCAATAATTATTCAGCCTTTTATACCTACTATTAACAAGCTTGCAT
TCTACTCCCAATTTATTGGGCTTTAACTCTATTTTGGCCAGCCACATTT
GACATTCCCTGAAGTAAATCTATGCTTTCCATCCTAAGTCAAGGAAGGAC
CTGGACTAGTAGGGCCAAGAAAGGTCTAAATTCATGGGTGGGAGAGAGA
GACTAAATCTGAAAGGAAGAATAGATTGAGCAAAGGTGTAGAGATTGGGG
AAGGCTGGACATTTGGAGAGAAGGAAAAGGAACTGACACTAAACCAAAC
AGTCTCACAAACACAATCTCATCCTTCCAAAACCTCTGTGAAGTAAGAATT
ACTATCCCAGGGCCAGGCACAGTGGCCCATGCCTGTAATCCCAGCACTTT
GGGAGGCCAAGGTGGGTGGATCACCTGAAGTCAGGAGTCAAGACCAACC
TGATCAACATGGTGAAACCCCATCTCTACTAAAAATACAAAATTAGCTGG
GCATGGTGGTGACACCTGTAATCCCAGCTACTTGGGAGGCTGAGGCAGG
AGAATCATTTGAACCTGGGAGGTGGAGGTGTCAGTGAGCAGAGATCGTGC
CACTGCATCCAGCCTGGGTGACAGGGAGACTCCGTCTCAAAAAAAAAAA
AACAAAAAAAAAAACCAAAAAAAAAAAACAAAGAACTACTATCCCAG
TTTTGCAGATGAGGCAATGGAAGCTCTAAAAAGTTAAGTAGGAGAAACAA
ACATGAAATGTATGTCTTATGCTTTTCCCTCATCCTATTTCCCTCAGCCTGG
AATGTCCATTCTCCCTCCACTATGCAAATCTAACTCTTCAAGCTAACACA
TAGCAATGTCTGAGAAACCGTCCCTGTGTTCACTCTGTTAGCCTCACTTG
CTCCCTCCCCATCCCTCTGTTTCTTTCTGTTATAACACTTCTCTATTCT
GCTGGCATCACAGTCATCTCCACCTGCCTTCCTCACAAGTTAAAAGCTTG
TTAAGGGCAAGTGGTGTCTTTGCCACCTCATTCCCCAGGGCTTCTAACA
CAGTGCCTCATGCATGACAGAGTTGTAAAACAGGTTACCAAGCTGGCTTC
AGGCAGGTTTGCATGGAAGTGTGCTTTACAGGAATACCTGCTCCCCCAG
GCCCTGGGTCTTCCCTCCTGAGTCCAGGCTCAGACTCTCTCATCCTGCTCG
TTCTCTCTTGGGGAGCCACAGTAACTTTGAGCAACTTTGCATGGGATAGA
ATGGCCTATTAGGGGCAGCACAAAGACCCCATGGAGGGAAGAGTACAGAA
AGGGAAAACGATAATCATATTTTTTTAAGATGTGCATTTTCTTAACAAAA
TGCTCTAGTACTTGTCCAGACTTTCAAACCTCAAAAACCTAAGCGTCCTTT
TCTTGAAGATCATCAAAGGCCCCAGTGGTCCCTCAGGTATGTCAAGCTTT
CTAGAAAATAAAGGTAAGTCATAATCACTTAACACACATGGCTAAATGGC
CATTTCTTCTAATTTATCAGCAACTGTTACATATTTCTATACTAGAAAA
AATTTATATTTATACTCAGGGTGGTAAGTTAAATTTGCCATCGAAGTAAA
GCAGAAAGAGCGTAGCATGTATGTATATGTAACCTCAACTGTGCATGAGAC
AAAGATGTCTTGAGGAGAATGAGTCTAAGATGCGCCTGAGCAATAGTACC
C

FIG. 3 (52 of 52)

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>Contig1

GCACCCATGTTTCTAAAGGGCATACCAGCCATAATAACAGGATGGGTGAG
GATATAGACAGCAGATGACAGAGAGGAGAGTGAAAGCTGGGAATCCCAGC
TAAAGGCATCAGGTTTATGGAATGAGTAGGGGACAATACTGTGTGTGTTT
ATACACACATGTATATGTGTGTATATGTATACATGTTTATGTATATATAT
AATTATATGGTACCATTTCTAATTGACAAAATAATCTATCACATTTTACA
TTATCAGATTTTACATCTATTGTTCTAAATACACTCAGTCATCAGCCCTG
TGTGTGGGCTCTTACCCATCCCCATGCACACCTCAGCTCAACCACTGATG
GATGGATCATCTGCCTATCAGAGGTGGCATATTCAGGTGAATCCATGGCC
ACAGCTGCAGCACTTCCTACCCACGCAGAAAGGCTCCACAAGAGGAGGCA
CACCCGCTCTGACTGTCCCTAAGCTCCTGACATCTTACCCCATGAAACT
GCTGCTCCTGGGTGCTTCCTGCCTTGCCCTGCCACCCCTTGTAAGTTCT
CACCATTGACACAGCTGGTGCCCGATGCAC

>Contig2

NAAAACGAATCGTCACTATTGAAGCCTGTCTCTCANC GGATCGTGACTAA
GAACCCCTCCTTGCTTCAAGTTGTCTGCCTTTCTAGGCAGAGCCACCC
TACATCTTAAATATATTGATTGATGACTACGTCTCCCTAAAATATATAA
AACCAAGCTGTGCTCTTACCAACTTGGGCACATGTGGTCAAGACCTCCTG
ATGCTCTTGTATGAGTGGGTGGGTGTTCTCAACCTTGGAAAAATAAACT
TTCTAAATTAAGTGAACCTGGGTGAGATTTTGGGGTTTACAGCAACAA
TTTAAAAAACTCACCATTGACCTGAAATTTTGACCTTATGCTGTTCTCA
CACTCCTCCATGAAAATAGACGCCATCCTATGAGTTCCTCAGCCATGTC
ATGCCACACTTCCAACATGTGTCCCCATCCACCATCTGTCTTCTTATTGC
TGCATCCTACCCAGGCCCTGATCTCTGGACCCATTGTTGTATAATTAAGA
ATTTGGGGCTGGGCATCGTGGCTGTGGCTCACTCCTGTGATCTCAACATT
TTGGGAAGGTGTATTAGTCAGGATTCTCCGAAGGATGCAACCCTAGGGA
TCCTCTCTATGACCCTATGTCTA

>Contig3

CGCGCTCAACCGACCGATTGCGCGAACCTGCCCATGCCCGAGGACAGTG
TAATCCTAAAACGTCCCCTGAATCATAAGGATATGAGTGCGAAAGTACGG
TTCCCTCTGTCAACCACTTTCTAACAACGCTATGTCCGATCCGTGCACTAA
CCCCGCCCAAGTCACTGAAACACTGATGGGCGCTTCTCTACAGGTATCC
AGGGCCAATACCACTACTCCCCTCCTCCTGTCCCCCTTCCACTCTCTAG
AGGCCGCGGATGCCATCCTCTATTAGCACAACCGAAAACGACGGTGAAAG
TACCACGAAGCTCACGATCTGATCGGTGCCCCAATGCGGTTACAACGGCT
GTCATCCCAACCCCCGTCCCATCCTCCATATTGCCCCCCCCCTATGAGGAT
GGCCCTATCATGACCTCCAAAATTCTGTCTCTCCCGACGTAATGCC
GCCCCCTCGAACGCTGACACCATCAAGTCNGTCACCTCCCAAAATACTCC
TCCTAATCACCAGGCCGAGTATCCCCGGTCCACAATACTCCTTGAGAC
GGGCCGATATCACACAC

>Contig4

NGGAGTTTAGGTCAACTAGTAACAAGTGGGATTGCGACTCAGGTCTATC
TAATCCTCAAACCCACGTCCCTGGACCCCTACACAGACTGCCCTCCCTCAG
TCCTCTGTGTGGCCTCAAGAAGGGTCTGGACATTCAAGTTTAAAAATCCA
TCCAAAGAATCTATGGACCCAGTGGTCTCTGGAGTCAATGTTCTGAGGCT
CAGAAGGGCCAGGAGGAGGGAGCCGCTCTACACAGTCTGAGCAGAGT
GGGCTGTGTCCCGGCACAGCAGGGGAGATCATAAACAGAATTCTGCCCTG
GGCCCTATTTAAGTAGGACCTTTAGGCTGCCGGTGTCTATGACCACAGGTC
CCANGTCTGCACGATTGGCTGTGTGTGGAAAATCTTCACTCCTTGCGGCC
TTGTCTTGGCAGAGAGACCGCTGCTTCTCTGATGGCCACCAGGGGGA
GGCGCTCCCCTGGGAACGGTTTGAANGGGAGCCTCACCCACACGTGCCT
TCCGTGGTACCCAGCACCAGCTGCTACCCATGGTTACCCACAGGCCCAGC
TCTGCTCTGAAGAAGGAGGAGTGGTGGCGATCANGCCTTGTCTGCATCCC
GTGGCTGCCCTTTCTTTTCTTT

>Contig5

GGGAGCTAACCGCTCACTGGGATTACAGGTACGCACCACCACGCCTGGCT
AATTTGTATTTTTAGTAGAGACGGGGTTTCTCCGTGTTGGTAAGGCTGG
TCTCGAACTCCCAACCTCAGTTGATCTGCGCCCTCAGCCTCCCAAAGTG
CTGGGATAACAGGTGTGAGCTACCATGCCTGGGCTTATATGTTTCTAGTC
CAAACATTTAGCTACCTTTTTTTTTTTTTTTGAGACGAAGTCTCACTCTGT

FIG. 4 (1 of 61)

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TGCCCCAAGCTGGAGCACAGTGGCACAAATCGTGGCTCGCTGCAGCCTCAAC
CTCCTCAGGCTCAGGTGATTCTCCACCTCGGCCTCCCTAGTAGCTGGGA
CTACAGGTACGCACCACTACACCTGCTAATTTTTTTGTTTTGTATTTT
TTGTACAGATGGGGTTTCTTCATGTTACCCANGCTGGTCTTGAACCTCTG
GGCTCAAGCAATCTGCCTACTTCAGCCTCCCAAAGTGCTAGGATTACAAG
CATAAGCCACCATAACCCGGCCTACCTACTTTTAACCTTGTGGAATTTTCTA
TAAGGTCANGGATGCCTGNNGGAACAAAAGTTTCTCCCTTGGTATATGCA
AGTAAAATCCACATGCTGCCTCCC

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AGGACTGTAGCTGTTGTCTAGTCACCAGGCTGGACTGCTTGGCATGATCT
CAGCTCACTACAACCTCCACCTCCTGGGTTCAAGGGATTCTCCTGCTTCA
GCCTTCCAAGTAGCTGGGATTACAGGCATGCACTACCATGCCCGGCTAAT
TTTGTATTCTTAGTAGAGACGGGGTTTCGCCATGTTGGCCAGGCTGCTCT
CAAACCTCCTGCCCTCAAGTGATCTGCCTGCCTCGGCCTCCCAAAGTGCTG
GGATTACAGGCGTGAGCCCCGGCCACATGTAAAAGTTTATATCTCTGT
TGTTTTACCTTGTTTTTGACCTAGTCTTTCAGTGATTTGAATCTTGATTC
AGTCTTTTGTATTTTAGTGGTACTTCCCAGCTTTGTGTCTATCTGTGGAT
GACATATGAGTCTTGCTTCTTCATGCCAATTTAAGAAGACTGAACGGGAA
TAGGTCAAAGGCATGGCCATGAGCGATTTCTCTCCAGCTTTTCATGGTGT
TCAGCTTCAAATCTATTACATATTGGACCTGCAAGCCATCATCTTATCC
ACAGGCTATCATAGGTGAATGTAAATTGGGTTTAGGTGGCCAAGCTG
AACGTGAGATATNTTC

>Contig7

AGCATGTCTCTAAAGGCCTATCAAAGCTGACATCAAAGGGATAAGTTCC
AGTTACCCAGCTGAAGGGAAGGAGGGTGTTCAGATAGAGGAAGGATAAG
CATGACCTATTCAAGGCCAGTGAAAGAAGCGTGCAACGGCCAAGTCAGGA
GAACCTGAAATTGTGTCAAAGAGCTTGGATGCAAAGAGCCGTGGGAGACT
ATTGGGGGTTTTAAGCAGGGATATAATATTCATTCAAGCATGCAGTAAAA
GGTCACTGGCACCTGCCATGGGCCAGGACTCGGGCTCTACATGATTGCGT
CTGTTTTGGAAATATCACCTGGCTGTGAGATGAAGAACAGGTAGGAGGG
TCACAAAACCTGAAGCAGAGAGACTGTTGAGGAAGTAAGCTGTTTTGTG
TGGACTGTGGCAATCACAGAGGCAGAGGATATAAATGCACAGAGACACAA
GGCATGTGGGAGGAGAAGGAATCAAATACAATGAGTGATCAGATGTGGG
GTTAGAATGGTGAGTGANAAAGACATACTCAAGGTGACACGCCCAGGTAT
CTGGGTGGATGGTAAGACATTCATGGACTAGAATCGAAGAGGAGGTGGGG
ATGGACATTCCTTCCGTTTAGAGGGGTTCCACCAGGAGGATTTGCCGGAAC
ATGGAGAGGATTAACCAGGAATCCGGTGCCTTTTTTCCAAACTGGGTGGA
GGGG

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GGTGAATGCTTTGGCACGCTGTGTAGATTTTAGGTGACGGGTGGTGACAA
TGAGTCCGTGTCGAGCGCTGATTTTTTCGGCCTTTAGAGCGAGATTTATA
CAATAGAATTTGGCATGAGATTGGATTGCTTTTAGTCAGCCTCTTATAGC
CTAAAGTCTTTGAGTGACTAGATGACATATCATGTAAGTTGCTGATAGGT
TTCCAGTTTTCCGCTCCTAGGTCTGCATATTGTACTTTTCTCTTACTCG
ACTTAACCAAGTACCAACCCAGCTTCTCAACGGATTTATACCATGGCACTT
TAAAGCCAGCATCACTGACAATGAGCGGTGTGGTGTACTCGGTAGAATG
CTCGCAAGGTCCGCTAAAATTGGTCATGAGCTTTCTTTGAACATTGCTCT
GAAAACGGGAACGCTTTCTCATAAAGAGTAACAGAACGACCGTGTAGTGC
GAATGAAGCTCGCCATAACCATAAGTCGTTTTTGCTCCCGAATATCAGACC
AGTCAACAAGTGTCAATGGGCTCGTATTGCCCGAACAGATTAAGCTAGCA
TGCCAACGGGATAAACGAGTCGCTCTTGGTGGAGGG

>Contig9

GGGGTGGGGCGCCTGGTGTTTTCTAAAGAGGATCTCCTGCCAGAAATGGTG
TGCTGACACTGTTGTCTCCTTGGTGTTGGAACCTTTGGTGGGAAGAAAGGT
TGGAAGGGAAATTTTGATCCTTGGATTAAACCCGAGTTTGTACTGATG
CTCACAAGACTAGGGGAAGGATAAAGGCAGGTGAGTCACTCTAGGATGGC
TCANTGAGCTCCACAGAGCTGGAACCACAGGCACCAGGAGGGATTACAGAG
CAGGCCTCAGTGACGTCAGCTGAGTGAACCAATGAGCAGGTGATGGGTC
CAGGCAGAGCCCTGTCTCTTTAGGCCAAAACCCCTGAAACACCGTTCCC
ATCCTAGCCTGTGTTCCACCCAAAGCTGGCCAGTCTCCAGGCCCTGCCTG

AGCCCCAAGGAAGTGGTATGGTGAAACAGAAGGGCCATTCTGTCCAATG
TGTGAGGAACTTCATTTTCACTTGTGGAAGCCCTGATGTTCAAAAACC
TCAATGATATCATTCAATTTTCCCATCCATTCAATGCCCATCCAATGCCC
ATCCGTTCAATGCCCTTCCATTCCTCTTCAGGGAAATGAAAATTGTTCA
GAAATCCTTTCTTTTCGAGAAACCAACCAAAACCAAAACCGCGAAATTCA
CTAAACTAGCCAAGACACAATCCTGGGTTATTTTCTTTTCCCAAACCTC
CTGTGTTTAAATTAATTCTACCTGTTTCTCGGCCCTTACTGCGAAGGTG
AACTCACCTAACCTCTCCCAAACAGAGAAGAACTTCTCTTGGTAAAATG
GGTTTTAACACTTCTAAAAAACCCCC

>Contig10

GCTATGGTTCTAAAGGTAATGGACTATGGCGTACACAACGTCTCGCTCAT
CGTCTGCCAGGAGGCTAAGGTATCCACGGACAATCGCTGAGCAACAGTGT
CGTTGATCCATCTCTGTACGCACTTGTCAACATGGCAGGAGTACGGGAGC
TGCGAGAATCCTCTCTGTGATGTCCCACGGAGCATGCCGTGAGACAACG
CCACGAACGGCCCTCGGAGANANCTACTCTGCAATGAAGACGTACGATAC
ACACGTAGGAGTCTTAGCTCACCAGCCGTATCTAGGTATACTGTACTCGC
GGATACTCACTCGTGCATGCGGCAATAGATCGATACGCAGTCGTACGCC
CATGCTCTCAGTGTGTGACCTTCTGGCGGTAGCGTNGTGGGCGCTATTAC
TGTGCGCAGCAGGCGCNTCGTACATGTGTGCGGTAGCGATGCCAGGAGCT
GTAACATAGCAAGTCGCCCCCTACTCCTATCACTATCCCTACGCTGGAC
CGCACTCGAGATCTGAACGCACGTCTTAACCTGCCAGTACTCGTGAGACC
TATACTGCGCAAGCCTTGGCTAGGAGATCCTGCAGCGCCGGCAAAGAATC
AGCTATGATCCCTTGGCATTATCGCACACGCACCATAGAGTATGTGCAT
ATTAACCTCTGAATGTGCTGCAAGCAGACGGTTGCTCAACATATATATGG
ATGTGGGAAATCGCCCTGGTCACCGCCACTTGGCGTCAGGAGGCACCAG
CACGTCTGAGTGTACGCACGTTACTC

>Contig11

GGCCGAATGGTGAATTCATCCGTCTCGAGGGGGTGAAAGACGGGGAG
TTATGCTGTAATGGCACCGCTCACCCCTGGGCTTATGAGCAGACCTAACCC
TCCANAGTGCTGGGATTACAGGCATGAGCCACCGTGCCCGGCCAGTAT
CTGAACCTCTGTGGCCAGGCAGAAAAGGTCTGTGTTACTCGTCTCCTTT
ATCATTGATGTCATATTTCTCCATTTGCTAACATTTATGTTTCTGCTCC
ACTGGATTCTTTGGATTTTCTAGAACATACCCATGCTTTGCATTGCCTT
GGTCTTTGAATATTTGGTCCACTTTTCTGCAAAGTCCCCCTCTCACCTTA
TCTTCTGTTAACTTCCAGCCAACACCTCTTTACTAACCCAGAGAAACAT
GGTTCAACTGTGCACAGGCTTGCACAGAACTGTTCTCATATTGTCTTGT
CATTGTCAATGTGGCAGAGATGCACCTTAGATACCTCTTTGAGAAAGGAC
TCACTGCCCAGCTGCCTGGCACGTGATGAGCTGATAGCTCCAGCTATAGA
CTCCTTTAGGGTCAACCTCTGCTTTCCAGTTGAGATCATATCCTTTGCAG
GGTGGCCTCCCCAGTGATGACTAAGGCAGTGTTACAATGGCCTAGTCATT
TCCTCCCAATGCTGGACTCCAATGAACCATCTGCTCCGGAGCTTCCAC
TGGGAGTCAGACCTTAGCTAGTCTGCCTCCGAATCAGAAGGCTCTCT
CTTGCCACTCTGGCC

>Contig12

GCTGTGTCTAAAGATTACGGCTGTAGTTCCAACCTCCCGCCGCCCTCTAC
TGTGTCTCTTAATGGCAGTCATTCACCATCTTCTGTCCCTCCCCTTCA
TTTCTTGGATGGTGACTGTCACTTTGCTGCAACAGAACCCTGTCCCAATC
CTTGATGGTTCAATACACACATAGACATTCTTTTAAACAGGGCGGCCTCT
CAGGTCTTTAATTTTCTTCCCTCCAATAACCTTGTGATGATCCCCAGCT
TAGCCACTTACTGCCAGATCATTACCAGTAACTCCAGCCCCCTCCTTAATT
CTAGTTTCTAATATCCTAATCTGTGACCTCACATTCCAACCTTCTTCATT
TTATCCCCTGAGTCAAAAAATCCTTTGATCCATGCAATCCATTAAGTCAT
CTACCTTTTCCATTCTTCGCCCCACTAGGGTTCTCATTCCTTTATTAC
CCATATGAAATTCCAAGGCCTGTTGGAATCACTCCCTTGCAGCCACTGTC
AATACTTCTGCCCTTTTACTTCATCACCTTATGTGGCAAACACACAGC
CCTGGTGGAGTCGATCCTTACCCCTGCTCTGTGCCAACAGCCGCACACGC
ATGGCTGATGGAGGTTGGAAAAATCCACACATGCAGTGGGCCCTGTATGT
CCATATACGTATCCAACCTCCAGCCTTGCATATGCCTCAGTGCTGCCTGA
CAACACATTATATGTTTCTTCTTAGTTCTTCTCAGTCTCCTGGGTGCCTAGG
TGAGTATCTCAGACATCCTTCTCTCTGCAAAGCTCCAACACCTCCACG

TCACATTCAACTGATGAC¹GTGTCTCCTATGTCACTTAGATCACAGAGGC
ATACATAAACAAATCCCAGCCACTGCCAGCACTCTGCACATCTGCGAGCA
TGGCACCCCCAATCTAGGCCTTTCTGTCTGCTCACTTGGGGTGAGCTGATT
ATACTCGATCCTAGTCATTTCTACTTATGCAC

>Contig13

CTTAAGGCCTCCCTCTAACATTTTAAATTAAAGATTGAAAAAGCAAAGATT
ATTCTGTTTTGGCTGCGCCTATAGTAAAGTAACCCCTATGNCAAATTTTG
ACACCTTATAGTATTTGACAGGGATAAGTATAAAATTGCTTGATTGATAC
ATCCACACCCAAATGTATGCTGGGAATGATTTTGTTCACGGCACTCATT
ACTTAATTTTTAAACTCTTATTTAAATTTGCAATGTTTTAAATGACCAT
CACTTAAAGTAGTAATCAACAGAGGTTAGGAGAACATAACAATACTCTTT
CTCTTAGAAAATACAACAGAAATATAATTTTTTACAGTTTGTCTCCCAA
CTTTTCTCTGTAATAACATGCCTTACTCACCTTTACAATAGGTTTGTGT
GAGAATCTTGTAATGTAAACCCTGGGTGTTCTGTGAAGCATTTTTTAACT
TCTAGTTTACACTGACTCTTATTCAAGTGTTTTTAAAAATATATTTAAAA
AACTGGCCAGGTGCAGTGGCTCACACCTGTAATCCCAGCACTTTGGGAGG
CCAAGGCGGGCAGATCACAAGGTGAGGAGTTGAGACCAGCCTAGCCAAC
ATAGTAAAACCTCGTCTCTACTAAAAATACAAAATTAGCTGGGCGTGGT
GGCGGGCGCCTGTAGTCCCAGCTACTCAGGAGGCTGAGGCAGAAGAATCG
CTTGAACCCGGGAGGAGGTTGTGGTGAACCAAGTTTGGCGCAATGCA
CTGCCAGCCTCTGCAGNGACAGCC

>Contig14

GGGGGCGGGCCGAGTGATCCTAAAGCCCGCTCGCTTCACAACAAAGCCTA
ACAGTCCAATCACTTAATGCTGCATTTATTCCTGGGAAGCAAGTCTCCT
TTGCACTTTACACAGTGAGATAATCAGTTTCTCATGTGGACCACTGGGCC
AGGAGGGCCTGACAAAGGGCAGTCTACATTTTCACTGGAACTGCTCCC
AGAACTATTTCTTTCTAGTTCCACCTCGGTCTGAGGTGCCTGAGGAGAG
GGACTCAACAGAGGAAGCAGGAGCATAGCTCAAAGTCTCAGAACATGGAA
GAGGAAAAGAATCCTCACAAGATTACGTAACCTACAGGCGTGTGCTGCT
TCAGTAGAAGTTTCATCTCCCTCAATCCTGTACACTTTCCATACATTAC
ATACTCAAACCTGGTCAGCCCTATGGAGCAATAGCAGCAAAGTTATTCTTA
ACAGTAATTAACAATAAAAAGATCCCATTTAAAAATGGTTACTGGTCAG
CCGGGCGTGGTNMNTCNANCCTNTAACCCCANCACTTTGGAAAGCATGCG
GGCGATCCCAAGTCTGATATCGAAACATCTGCCTAACATGTGCAACCCCT
CTCTACAAAATACAAAAATATCCGGGCTTGTGTTGGCGCCGTTATCTCA
CTACCCGGAGCTAAGTAAGAAATGCTTTACCTGGAAGCGATTTTTTTACT
TATATCCCTCTCTTACCAGGCGCGACCAAATCTTTAGTATAGGAAAG
TTTATTGTTTTATGCCTTTGTCAAGGCTCTACTGTATCTTTTCTGTCCAC
TCAC

>Contig15

GGTCTGAACAACAGCAGGCGATTCTAGCCCTGTACCCGGGGCATTGTC
CAACACTCGACAGGGCTGAATTCGTCCATAACGGTGTGCCCCCTCTGGGAT
ATAGGATGAAATGAATTGATCTGAGTACCTGGGATGTAAAGTTACTAAAA
CGCCAGCTAGGTTACGCCCCGATGCTTAAATATGATCGTGGCCTACACC
TCGTCCAGCAGAAAAAGTACCCTTTCTTCAACACCACCTCACGATCCTCC
AATTTAGGAGCTATAAACTCATGACTCTTTATTTACCCCTGCAGATTCT
TCAATCCAATAGTGTGTGTCTCCCTGTGAACTCACGGATATACCGATTTT
CCCCACGTCAATTTCCACACGTGCAATCGCTTAGTCATCCCTATGTATGA
GAATCATGGATGACTATGTTGAAGTCCATCTATAAAGTTCAACCCCCATC
TCCGTCCCTGATTCCCCCTCCCCAAGATCACCAACGCGACTCGACATATT
GTTATCGCCCAAGGGACCTCTTGATCCCCCATATCCACTGGTCACCTCC
CCTCTTGGCTGGAAGTCACCGGAAGTTCTCCACATGTTGT

>Contig16

TGCGAGCGATGTTCTTAACTTTAGCGCCATTGACTCGAGCATGGTCATG
GCTGTTTCCTG

>Contig17

AGGGTGTTCTTAAAGGATACTACGTTCCCTAAAGTCCAGAGAAAAA
AAAGTAACATAATGTGGCTTATTTGGTATAAAAAATTTTACAGGAAGCATT
GTCAAATATGAAATAGTGTGTTGGTTTTGTTGGGCTGTATTTGTATAAAT
ATGTTATTGGTATGTGTTCCAAAATTATAGGAACTCCTATAATTCTGAT

ATGACTTGGTGTACATTATCAGTAATAATTATAATTGTTATGGTAAATTA
TTGTGTGCCATGGAGGTAACAAATTTCTCATCAAGTGTGTCTTTGACTA
TGGTTGCCCTAAAACTTTTTGCCATTACAGACAATTGTCTTGCTTTGGT
CCTCTTTAGAAGGTGGTTTTATAATCAGCTATAAACTCTAACGGGTGCT
CTTGAATGCAGGCTTAAGATAGCTTTGGAGACTGTGACATCAGAATAGAG
GAAAACTTTTCACTATTTCATGGAGTGCTGAAATATTCATGAATATCAAGC
AAACAGGAATTAACCTTCATAGATGGAATAAAAGAATGCTGAAGTAATC
TTTTTGACTTTTTTTCTTAAATGTTGATCCTTCGTTTTGTTTTTCAGAG
TCAAGGAAATTTTTCTGTTGAGATATTGACAGCTTTTAAACAATTAAGTAT
ACTCCAGTGAACACAATTTGGAGCATATTTGTGTCTCTCTATATATATTT
GGAAACAATNTTTGAGTATTCTTAACCTATTGCAATATT

>Contig18

GGTTGTCTGCTATACCAGTAATGGGATTGCTGGGTCAAATGGTATTTCTG
GTCCAGATCCTTGAGGAATTGCCACACTGTCTCCACAATGGTTGAACT
AACTGACACTCCCACCAACAGTGTAAGCATTCCTATTTCTCCACATCC
TCTCCAGCATCTGTTGTTTCTGACTTTTTTAATAATCGCCATTCTAACTG
GCATGAGATGGTATCTCATTGTGGTTTTCAATTTGCATTTCTCTAATGACC
AGTGATGATGAGCTTTTTTTTCATGTTTGTGGCCACATAAATGTCTTCTT
CTGAGATGTGTCTGTTTCATATCTTTTGGCCACTTTTTGATGGGTTTTTTT
TTCTTGCAAATTTGTTTAAATTCCTTGATAGATTCTGGATATTAGCCCTTT
GTCAGATGGATAGATTGAAAAAATTTTCTCCTATTCTGTAGGTTGCCTGT
TCACTCTGACAATAGTTTCTTTTGTCTGTGCAGAAGCTTTTCAGTTTAAAT
AGATCCCATTGTCAATTGGCTTTTGTGCAATTGCTTTTGGTGTCTAA
TCATGAAGTCTTTGCTCATGCCTATGTCTCTGAATGGTATTGCCTAGGTTT
TCTTCTATGGTTTTTATGGTTTTAGGTCTTATGTTTAAATCCTTCTTTTT
TTTTTTTTTTTTTTTTTGAGATGGAGTCTTAGTCTGTTGCCCAGGCTGGA
GAGCGAGTGGCGTGTCTNTAGGACGC

>Contig19

GCATGTTGTCTAAAGGTTTGTCTTCTCCAAAATTCATATGTTAAACCT
AGCCCCAAATGTGATAATATTGAGGAAGGCTCTTTGGGAGGCAGAGCC
CTCATGAATGGGATTAGTAGCCTTATAAAAGAGACCCCTGAGGGCTCCCT
TGTCCTCCCTCCACCGTGAAGGATGCAACAAGAAAGTATGGTCTATGATCC
AAAAAGCAGACCCTTGCCAGGTACCCAATATGCTGGCACTTGAACCTCCC
AGCCTCCAGAATGTGAGAAATAAATTTCTATTTTTTCATAAGCCACCGAG
TCTATGGTATTTTGTATAGGAGCACAACAGACTGATGTGCCACCCAAC
CATGATTATACGTGTAATTTATGGTTTTCTCTGCTAGTAGGGATGCACCAT
GGGGTTAGGAACCACGCTTTTCTTATTTCCACACAGTCTTAGCTCTAA
GCATGTTCTGAATCAAAGATCCCCATCTTTTATGAATGAAGGAGTCAGT
GAATGAATTAATGAAAGAACTGATAACCTCAATAATTATTCAGCCTTT
TATACCTACTATTAA

>Contig20

ACGGTTCTCTAAAGACTTTCAAGAGCTGGATTTTATGCTTTAGGTGAAGG
TGATAAAGTAAAGTGCTTTCAGTGTGGAGGGGGCTAACTGATTGGAAGC
CCAGCGAAGACCCTTGGAACAACATGATAAATGGCATCCAGGGTGTA
TATCTGTTAGAACAGAAGACACGAAAATATATAAACAATATTCATTTATC
CCATTCACTTGAGGAGTGTCTGGTAAGAACTGCTGAAAAAACGCCATCAC
TAAGTAGAAAAATTGATACCATCTTCCATAATCCTATGGTACAAGAAGCT
ATATGAATGGGGTTTCAAGACATTAAGAAAATAATGGAGGAAAA
AATTCAGACATCTGGGAGCAACTGTAAATCACTTGAGGTTCTGATTGCAG
ATCCAGTGAAGGCTCAGAAAGACAGTACACAAGACGAATCAAGTCAGACT
TCATTGCAGAAAGAGATTAGTACTGAAGAGCAGCTAAGACACCTGCAAGA
GGAGAAGCTTTGCAAAATCTGTATGGATAGAAATATTGCTGTGTTTTTA
TTCTTGTGGACATCCAGTCACTCGTAAACAATGTGCTGAAGTGGTTGAC
AAATGTCTCAAGTGGTACGCAGTCATTCTTCAAGCAAAAAAATTTAT
GTCTTAATCTAACGCTATAGTAGGCATATTATGTTTCGTATTATCCTGATT
GAATGTGTGATGTGAAGTGAATTAAGTAATCAGGATTGAATTCATTAG
CATTTGGTACCAAGTAGGAAAAAATGTAAGCCAGTGCTTAGACACA
GC

>Contig21

CGCTGTCTTAAGAACTGGGCTAGGAGTGAGCAGTGAGCCAAGATCGCACC

ATTGCACCTTCAGCCTGGGCAACAAGAGCAAACTCCATCTCAAAAAAATA
CATATATATATATGACCCATAAAAAGGAGATAAATCAACACTTCAGAACT
GACCCAAACTTGGCAAAGATACTATAATTAACAGAAAAGGACAGTTTACTA
AGTACTCCGTATGTTCAACAAGTGAAAGATTAAACATATTAAGTAGAGAT
GTAGAAGATATAAGAAGATCCAAAATGAACTTTTAGAGTTGAAAACTACA
ATATTTAAGATAAAAAATACACTAGGTGGGATTAAGTAGATTACACATT
GCATAAGATAAAAAAAATGAGCCTGAATACAGCACAGTATAAACTATCT
TAAACAAAAACACAGAGAGAAAAATAACTTTAGAGACTTAGCTCTTATC
CTCTATTTGTTTTCTAAACAGAGGATAAGGGGCAGAAAAAATGTTTGAAGA
AATCATGATTTTTTAAATTTCCAACCTGAGATAGGAATAGCACTGGGTAGTC
ACAGGAGGCTGGAAAGACCCAAACAGCAGTTAAACAGGAACTAGGCAAA
GAAACCAAAGGATAACAGTAAACCTAACTAAGGGAGAGAAAACTGACAA
AAGCTGACTTAGGATAACTGAC

>Contig22

CCTGAATATAAGCCGCAAGTAACCAATTAAATTTGTTTTCCAAAATTGTA
TTAACAATCTATGAAATTTTTATCTTGACCATAGCTATAACTCCAGAAG
CCTTTTATAACCTCTATAACCTTTATTAAGGAGTAGGTTAATGCTTCAAG
AAAACCTTGTTAATCTGACACAGGACCCATATGCTGATCTGTCATCAGTG
TGGCTTGGACATCAATGATTATGATTAATTTATAGAGAAATTGAACCTTAT
TTTATCTCTCAAAATTGGCCCTTACAATCTCACACACCCACCTCTCCAC
TATAGTTCCTGGGCCTTGAGTTGAATAGCTTTAATTTCTGGCTCTGTGTT
TCAAGAATGCAGTTTATTTTGATTGGCATTCTTACCAGTCTGAAGATG
AACCTTTAATTGCTGTGTCAGTATTTAAGATTTAGCAGGACTTGTCCTTTTA
AGAACCAGGAGTCAAGCCCTATAACTCAATGTCACAAGGACTTTAAAAGC
ACATACATAAAGATATATGGATGTAATAATCATAATTTTTAAAAAATTGT
ATTAATCTCAGTGTTTTCTAAGCAAACCAAACTTAATAATAATGGCATA
GAAATTATTTCAATAAAACATAAAATCTGTTAAGCCAGTTACCAAAGGC
AAAAGAAAAGACCTTCTGCAATGCACAGAATATTATGTTGGAAGAAAACA
TTTCCTTTAGACCTTTAAGAAAACATTGTTAGCATCAGGACACAACAAAC
AGAATCTGAGGGTAAAAAACGTATATGAGCTGAAGGGAGTTGAAGGAGGG
CATTACTATTTCCACCCCTTTTAAAGGGGAGAGAAAACCTAAAACAGCAA
GATGCAATAAAAGCTGAACCTTTGGGTAAAAAAAATTCTTAAGTCTCTT
ATAATTTATTAAGAGTGAATCAACCCCGTAAGAAAATTTCAATTGTTCTAA
CCAATTTTTTAATATATAAGTAGTTTTTTAACATCAACCCAATCTCTAGA
AAGACCATTATAATTCCCTTTAATTATAGACAACCTTTATCATATAAAAG
TTTTTTTTAAATAAATCCTCTTATTGTGACTTACACAGACTATTCATGACA
TGCTTGGACTTTCTGGTTTGTGCGTGAACATCCTTTCTTTCTTTCTTTCT
TTTTTAAATTTTACTTTACGTTCTGGGATACATGTGAAGAACATGGAGGT
TTATTACGTAGGTGTACATGTGCCATGGTGGTTTGTGTCACCCATTAACC
CGTCATCTATATTAGGTATTTTTCTAATGTTATCCCTCCCTTGCCCCC
CACCTCCTGACAGGCCCTGGTGTGGGACATCCCTCCCTGTGTCCATGTG
TTCTCAATGTTCACTCCCACTTATGATTGAGAACTGCAGTGTGTTTTGTTTT
CTGTTT

>Contig23

GCTAAATATAAGCTATGATAAAACAGTTGGCCCTCTGTATCATGGGTTTC
ACAACCTGTGGATTCAACTAACTGTGGATGAAAATACTTGGGAAAAAAG
AATGGCTGCATCTGTACTGCACAAGTGCGTGCTTTTATTCTCGTCATTAT
TCCCTAAGCAATACAATATAACAACCTATTTATATAGCATTACGCTGTAT
TAGGTATTATAAGTAATCTAGAGATGATTTGAAGTATACAGGAGGATGTG
CTTAGGTTACATGCAATATTATGCCACTTTATATAAGGCCCTTGAGCCT
CCTCAGATTTTGGTATCCATGGCAGTCCTGGAGTCAATTCTCCTGCAACA
TCTCCATTTGTTTCAGATTCTCTTCTATATCATGTTTATATCAGAAAATCT
ACATAAGATTTTTTAATGTGTTTCATATAGGTTTTGTGTATTTTTGGTTGT
TAATCCCTAGATATATGCAGTATTTATTGCTATTATGAGTAGTGTTCCTT
TACCATGTATTCTAGTTGGTTATTGCTGACAGAGAAATGTTGCTGGTGT
TCTAAGTTACCTTGTTTCTAACAACTTGCTGAACTCTTATTAGTTCTCA
TAGTTTTTAATAATCTTTCTTAGTTCTGATAACATAATCTGCAATAAT
GACAATTTTATATCTTTCTTTCCAATGCTTATATCTCTCAGTCCTCTTA
TCCCAAAGTATTTTCCAGGATCTCCACTATAACATTAAATAGTAATAAGA
ATTTCTGTCTGTTACTGATCTTAAGGAGAATAAATTTAAATTTCTCTG

FIG. 4 (6 of 61)

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TCAGGTTTTATGCTTGATATAGATTTGTGATATATAGCCTTTTCACAGGT
AAAAAAAAAATGCTTTCCTAGTAGTCCTAATTTTTTAAAAAATCATCATA
AATAGATGTTGAACATTATCAAATGCTTTTTCTGCATCTATAGAGATAAT
CATATGGTTTTTTACTATTTATTAATGTAATGAATTAGACCAATTTTCTA
ATGCCAACTCTTCTTGATTTGTAGGGTAAATCCTATGGGATCATAAAA
TACTTTTAATACATTGTTAGATTTGAAGAGTTAACGCCTTATTTAGAACG
TTTTCAGTCACATCCATAAGTGAAATGGCACTATAGTGTCTATTACTATT
ATATTTTCTGGTTCTGAAACCAAATTTATACTCACCTCATACAGTAAGT
TGGGCAACTTTTTGTTCTTTTTTCTGAAACAATTTGTGTATAGAAGAAAT
TAAGTGTTCCTTGAAAGTTTGATAATAATCATCCAGAAAATTATCCCCAT
CTAGGGCTTTTACAAAAAGGAGACTCTAGAATGCCATTTTCGGTTTCTTG
ATGTGTATTGGCCTCTTTCATTTAGGCTTTTGGATTTTTTAGGGCATT
TTCATATAGGCTTTTACCGG

>Contig24

CATAAAGTTTCAGGTTGGATGTTTCGGTCAAAGTGGTCCGGCGATGCGAAAA
CGAGAGGGCTCGAGGACTGGGCAGAGAACTATTTGAAGGTATCTCTCAGG
GGAAACCAAGCGGAAGGCGGGAGTAAAATTGGGAGGGAGCGACGGCCTT
CAAAGAAGGGCTTGCAATTAGATCGGCGAGATCCGGGAGGGTCTGGTGGG
GAGAAATGACTAGAGGACAAATCTAATGGAGAGACAGACGGAGATAGATA
TCGTGACAGAGAGAGGGACAGTGACAGCGCACACAGTGCAGGGTCCATG
AGTACAAGGCCCTTAAGTGTACACCCAGCCGAGTGCATGGCAATTCGAT
TCCTGTACTGACCACCCAGGATTTGGGTAGACTGTACGAGTTAATGAGCA
TGGTCCCCAACAGACTGCTTCGACCTCAGATGCAAAGCACACTTCAGGG
GTCCCCAAGCCACTCATGTTTTTTGAATGACTGCCATAAGTTCAAAAATT
CCCACAATTCTCTCAGATTCATAACTGGGTATAACCACTCATAGAACTC
AAGAAAATGCTATCATTATTATTACAATTTATTATAAAGGATACAAATC
AGAAGGACTAGCCAAATGAGGAGACACATAGAGAGAGGACTAGTAAAAAA
CAGAGCTTCTGCGTCTTACCTTCAAGGAATCAGGATGCACCACCCTCCCA
GCACATCAAGTGCTCATCAACCAGGAAGTTCCTCTGAGCTCCAATGTCCA
GAGATTTTAGGGAGGATTCATTACATAGGTATCATTGATTAAATCATTGG
CCATGTACTTGAACCTCAATCTCCAGTGTCCCTCTTCTCCCTAGAGGTCTG
AAGGGTTGGCTAATATCATGTGGCTCAAAGCCCCAACTCTAATTACCTTT
TTGGTCTTTTCAGGGACTAGACCCCATCCTGAAGCTATCTACAGGCCCTG
CCATGAGTTAGCTCATTAACATAACAAAGACACTTATATTACTCAGAAAA
TTCCAACAGTTTTTAGAAGCTCCATGTCAGGAACCTGGGACATAGATCAAA
TTCTTTTTTTTTTTTTTTTTTTTGGAGACAGGGTCTTGCTGTGTTGCCAG
GCTAGAGTGCAACGACAGATCACAGCTCAATGCAGCTTCAACTTCCCAGG
CTTAAGTGACCTTTCCACCTTAACCTTCCAAGTATCTGGGACCAAGAAA
ATGGCTAATTATCTGCTGATTTTTTAACTTTTTTTTTTTTGTAGGGATG
GGATCCGCTGTGTTGCCAAGGTTGGTCTCAAACCTCTGGGTTCAAGCAA
TCATTCTGCCCTGGCCTCTGTGATGGTTAATACTGAGTGTCAACTTGATT
GGATTGAAGGATACAAAATAATTTTTTGGGTGTGTCTGTGAAGGTTTCG
CCAAAAGACATTACTTTGAGTCAGTGGACGGGGAAATCCCCCTTCCCCA
TGGGACGGGGAGACCCCCCTCCATCCAGGTAAAAAATCTAATCACCTGC
AATGTGGCAGAAATAAAGGAGGGAAAAAACGGGGACCCCTANATGGGTTA
TTCTCCACCTAATTCTTCCCCCAGG

>Contig25

CCATGTATTTCAATTTCTACAGACCCTGAGATGAATTTGTCATTGCCACGG
GGTCTGAAGTTCAAATACTCTATTTGGTATCCTGCCCTGTGGTTAACT
GTGATCAATTTCACTCACCTTGTATTGATGAGAGGTGCCACCATCTGGCC
TCCCTCACTCTGCAATCCTGTTAATTCCTATCAAAGCTGAAAACCTGCTG
CAGCACCCACACCATCACCTCCAGCCTAGAGAGGGAAGCTACCAGTGAGC
TCTCCTGGATGCCGGTGTGCCCTCGCCAATACATTTCTTCTTAGTCCCT
TGGTCATCCTGAGGTGTGTGATTAATGGACAGCTATGTGGATTGCACATA
ATAGATGTACTCCAGCATCTTCATCCCTGATTTTCCTTTACAGAAATCAC
TCAACCTTAGCAACATGTGAAAATCACCTAAGGACATTCTTTAAATCCCT
CTGTCCACATGGCAACACAAACCACTTAAATAAGAATCTCCAGGGAGTCA
CTCAAGCATCAATGTTTTTTAAAGCTCCAATTTTAAGGATCATTACATTA
TGTCGAAGAAATTATAGTATTTACGCTTACTGACTGTAAACCACCACCA
TATCTAAGCATCCATTAGTCAACCTAGCAGACAATAAACTAACATTACCT

FIG. 4 (7 of 61)

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CCAGGTACTCAAATCAATTCATTGCATCCCAAATCCCAGATGGGCCCACC
CTTATTGACAAATTAGCCCAATCTTGGTTGAACACATTTAGAATATATT
TCCATGAACAATATCCGGTTGACGAGTTTCTTTAACTTTTGGAGTTTAA
GCCATTTCTTTTACAGTAGCCTTGTTAATCCCTGTCAATGCTCCATGG
GGGTCATGAAGAGACCTCTTATTAAGTGTGAAGCAACTTGGCTCAGGTGC
AGACACTCAAATGCTTCACATGCAGTGGGAAAAGAGAGTGATTGTCTAC

>Contig26

TTTAAAAAGAACTGAGTCTTTATTTCAGTCGATTCTTCTAATCTATGAACA
TAGCATCTCTCTCAAAGCATTTAGTCCTTCTTTAATTTCTGTCATTAATT
TTTTAAAAATTTTCATCTAAAGATTCTGTATATGTTTTGTTGAATTTATG
CTTAAGCATTTCACCTTTCTTGGTAACAATTATAAATGATTTTGTGTTTTT
TATTCCACTAGTTCATTTTCAGTGTGTAGAAAAGCAATGAATTTTTGTGT
GTTGATCTTTGTTCCAACATCTTGCAACATTATTGAACTCATTATTAGT
TCTAGGAGGTTTTTTTCATTTTTCTTGTAGATACCTTGAGATTTTCTATAT
AGACAGTCATGTTGTCTGCAAACAGGCACAGTTTTATTCTTCCTTTTCA
ATCTATATGCCTTTTTTTTTTTTTTGCCTTATTGCAGTGGGTAGAACTT
CTAGCACTATGTCAAATAGCATTGGTGAAAGCAGACATCCTTGTTCCCTTG
TCTTAGAGGAACATTTGGTCTTTAATCTTGATTTAAAAAATTCCTTGCAC
TAAGTTACCGTGTTTTGCGGGAGGGAGAGGTGGGGTGAGGTGGGGATTTC
CCCTAATGTTTACAAGCTGGGATTTTCTTTTCTGTGTCTAATTATTTT
CCTCATTGGCTTGAAAAATCTGATAAAACATTTTAGGACTGTGTATAAAA
TAGAATTAGCCAAGTGCAATGTCTTTATTTCAGAAGAAATTTTCATGGACGT
TGTGCCTACTCTCTTGGCTTCTGGCTTCATGGCTTTCCAGATCCCACAG
TAAGCTCTGGATAGTAGAAGTTATAGTAAGACTGACTTCTAAATAAATGA
AGTGACTTTAACCTTACTGATATGGCTTAAAGAAAAGGAGTGGCCTTTAA
GATCCATGAACCTCTCAAACAAAAGTGATAACGTTATCTCCATGCATATA
TAATACTAAATATAATGCAACTGAGAGAAGTAGGCTGTGGTAAGAAAGGA
GACCCAAGTGCCATCTGAAGGCAGCACTTACCACTCTGCTTCATCCCACC
GAGGAAACAAAGCATGAGTATTGCCAGATTTTCTTCTGTTTCAAGAAAAG
CCAGAAATCCAGGTTTTTGCCTGAAATGTCCTGATTTTAAATGTTGGGAAC
TAATTTATATTTTGAATAACATTGTGTGGGACAAGTGAACCTGTATGTG
GAACTGCTTTCTCCAGTGGCGACCAGTTTGGACCGTTGATACTCAGCAA
GTTCCGCCAAGTGCGCCTTGTCAATTGTCAAGTCAAGGTGATGTGTGAT
TGGTCAAGCAATTAATTTTGCTCAGCATCTCGTGTGTTTTCAAAGAAGT
GAAGGTTCAATTGC

>Contig27

TTTCAGAGCACAAATGCGTATTTCATAGTATATTGACTTAATTTCTAAGTGT
AAGTGAATTAATCATCTGAATTTTTTATTTTTCAGATAGGCTTAACAAATA
GAACATTCTGTATATAAATGTGTAAATTAGAGTTAATCTTTCCAATCACA
TAATTCGTTTTATGTGAAAAGGAATGAACGTGTTCCATGCTGGTGGAAAG
ATAGAGATTATTTTAGAGGTTTGTCTGTTGTGTTTTGGGATTCTGTTTTT
TTTTAAATTTGAAATATGTACTTGTGTGAATGATTTTTTAAATGATTT
TACCATTTTTTGGAAGGGTATTTAATGATAGAATATCATCGAGCCAACATG
CACTGACATAGAAAGATGTCAAAGATATATTAAGTGTAATGCAAGAGG
GAAAACACTATGTACAGTCTGAGCCAAATCAAAGCATGTATGTTTTTTAT
ATGTGTACAACAAAAGGTTTGGAAAGATATGCGCCGAATTGTTAAATGTG
GTTTCACTTGAGGGGGTGGGAGGATGGGGCCCCAGAGGGGTTTTATGGG
GGCCTTTCACTTGGTATTTTTTTTCATTTTGTTCTGTTTGAAATTTGTTT
TTTCTTTTTTAAATGGAGTTTCACTCTTGTGCGCTAGGCTGCAATGTAGTG
GCGTGAACCTCAGCTCACTGCAACCTCCGCCTCCCAGGTTCAAGTGATTCT
CCTGCCTCAGCCTCCCATGCCTCCTGTGTAGCTGGGATTACAGGCACCCA
TCACCATGCCTGGCTAATTTTTGTATTTTTCAGTAGAGATGGGGTTTCACC
ATGTTGGCCAGGCTGGTCTGTAATTCCTGACCTCAAGTGATCCACCCACC
TTGGCCTCCCCAAGTGCTGGGATTTTCAGGTGTGAGCCACCACGCCAGCC
CTGTTTTAAATTTTTATAAGTATGTACTACTTTTGTAAATCAGAATTATTA
GAAAGCATTTTACTGATTTAAAAGCTTAGACATGTTCAAATGCCTGCAAA
ACTACTTAACACTCAGCTTTAGTTTTTCTAATCCAAAAGGCCGGGCAGT
TAATCTTTTTTGGTGCCAATGTGAAATTTAAACGGTTTTTATGTTTTTCTG
TGTTGTGAATGAAAAATATTTCTGAGTGGTGGTTTTTTGACAGGTAGACC
ATGTCTTGTCTTGTTCAAAATAAGTATTTCTGATTTTGTAAATGAAAT

FIG. 4 (8 of 61)

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ATACAATATGTACAGATCTTCCAATTAAGTAGTAAGGGTTTATCCTTAA
TCCTTGCTAATTTAAGCTTGCATAAGTCACTTTACTAAAAGATCTTTGTT
AAGCTAGTATTTTAAACATCTGTGAGCTTATGTAGGTAAAAGTAGAAGCA
TGTTTGTACACTGTTGTAGTTATAGTGACAGCTTTCCATGTTGAGGTTCT
CATATCACCTTGTATCTTGAAGTTTCATGTGAGTTTTTACCATTAGGATG
ATTAAGATGTATATAGGACAAAATATTAAGTCTTTCCTTTACCTAAGTTT
GGTTTCTTGACTAGTAATAGTAGTAGATATTTCTGTAATAAATGTTCTCT
CAAGATCCTTAAAATCTCTTGGAATTTATAAAATTATTGGAAAGACAAGA
ACAGTTTTTATTTCATTATATGCATTATTATCG

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CTTTCTCAAGAAAAGGGAAGTGGAGCAATTAACATATGTAATTTTTTTT
TAAAAAACCTAAACCTAAACATCTACCTATATACAAAAATTAATTAACA
ATGGATCATGGACTCCAATGTAAAACATGAACTCTAACTTCTAGAAAA
AAAAGTGGAGAAAACCTTTGGTACCTATGACAAGGCACAGTTTTTAGACT
TAACACTAGAAGTGTGAACATATAAGAAAAAATTAATAATTTGAACCTT
ATGAAAATCAAATTATTTGCTCTCCAAAAGACCCTGTAAAGAGGATGAAA
ACTAAATTACAGATTGAGAGAAAATATTTGTAAATCACATATTTGACAAT
GGACTTGTATCTAAAATATCTAAAGAACTCTCAAACTCAACATTAAAAA
AAATATCTAATTAGAAAATGAGTGAACATTTTACGAAAGGGGCCTTAGA
ATTAGCAATAAAACACTTGAAAAGATACTCAGCATCACTAGCCATTAGA
AAAATGCATATTAAAACCAATAATGTATCGCTACACACATATAAGAAT
GGTTTATGAAAAAATAGTGATGACACCAACTGTTAGTGAAGATGTGGAGA
AACACTCATACTTGCTGGTAGAAATGTAAAATGGCAGCCACTGTGGA
AAATTATTTGGCAGTTCTTTTAAAACCTAAAAATCAATCTACCACACAAC
CCAGCAATTTTATTACAGGGCATATATCCAGAGAAATGAAGATTTATGA
TCACACAAAAATCTGTACACAAATGTTTTATGGTCACTTTATTTCATAATA
GCCAAAACCTGGAACTATCCAAATGTCCTTCAATGGGCAAAGGATTAAA
CACACTGTGATACATCCATACCATGGAATACTACTCAGCAATAATAAGGA
AAGAATTACTGCTACACACAAGTTGGATTAAACTCAAGGAAATTGTGCTG
AGTGAAAAATTAACAAGCCAATCTCAAAGGACACATACTTCATGATTCCA
TTTGTATAACATTAAATTAACACAATTAATTACAGAGATGGAGAACAGAAT
AGTGGTTGCCAGGGATTATACATGGTGGACGCGGTGAGGCGGGCCTCCAC
GCCTTGAGATGAAGGGGGCTACACCCTTTAAAGCACACCCACGAGAGAG
TTTTGTGCGGAGGGGGCCCAATTTAAGTACTCCGCCCCGGGGGGGAACAC
AGGGGCAAACAAAAAAATTTGGCCTTGGGGGTGACCAAACACAAAAAA
AAAACAAACACAAAAAAACAACNATGGGTGGGAGGATTAATCGCCAAA
TCTGAGTAAGCTATCTGGACAGTACCAATATCGATTTCAGTTTTTGATG
TTGTACTATAATAATGCAAGATGTTAACATTGGAAGAAGCTGGCTGAAGG
GGGCTCAGGAACCTCTCTGGACATTTCTTTGTACCTTCCTGTGAATCCATC
ATTATTACAAAATAGGACATTTTCTAAAGGTTAAATCATTTTAAATTTAA
AATGTCCTGTTACTGTTGAAACTCACATCTCCATATACTGATCAAGAAC
AGCACTAATGGCCCTGGCCTCCAGGAATTCACAATTCCTACTGACTTTT
CTTTGAAACCTTGCCCAAGTCGCTTCTCTTCTCTGGTCCTCAATTTTCA
TCTTCAAATGAAGATTGAATGACTATTAATCTCTTGCAATTCTTGAG
ATGAAGGGTCCTAAAGGAACTGAAGAGGATGCCATGTAATGTAAATATGG
GTTTTTACTCCATCAGCCAGCCAAGACAGAGGGCAGACACCAAGACATGG
TAACCAAGGAGGCCATGTGTAACAAAGACCATTAGACTTATGCTCTGG
CCTTTGCAGCCCAACTGGTGTGGCCAGTTGGTGGGGTATGAAGAAAATGG
GGCCTTCCAGGAACCATGTTGAGTGGAGATAAGCAGGGAGGAATGCAGAA
GACATGGGGGCAGTGCCAGTCTCAGCCCGAGCCAGCTACACCCACACATG
GTTATGAAAGACTGACAGCCTGTAAGNTGAACACAGCCCTGCCTCTCTTA
GATAGGC

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GCAAATATGATCTCAGATGTGGATTTACTGTAAAGTTCATCAAATTTAAA
TTTCAGAACACTTAATCTGCAAGAGTCCTTTCCAAGACCCTATACCTAAT
TTTGTGTTTACAATTTTATATTTGTTTTCTTAAAGAAGACCACCAATATA
AACTATATCCAGCCTTCATGATAAGTACATAGGAACTATGCAAATAAGG
GGGAAAAAAACAAAGAAAAATACCTAGTTTACTAATGGTTCACCTTCTGA
ATAGCACATATTTCATAATGATACAAGCACTCATTACTAGTCTAGGAAAT
GAAGATATAATTGCATTAGGAAGATCAAGAGGTAGGAAATGTGGATGTGT

GTGGTATAGACTAGGGCAGGACAAAGAACCTAAATCCTCATTTTTCTAAAG
ATAATTGTTAATACGTAAAACTCAAATTCAGAAGTAACAGTAAAAGCG
GTCATTAAGAAACAAGCACTAAACACCAGATAGGAAGCGAGAGATGGGGG
AAGAGGGCGACAATCTGATTATTTTTTGCAACAAATTTTGTAACCATT
TGACTGTTTACATGTAGAACTTGGATCTTTTTTAAAAAACACAAAATAAT
AATACTATTATTTTTTAACTGGATTTTTTGAAAAAGAAGATAAAAGTCTCA
TTTAGTAATTAACCTCATTCCAGGTAGTCCACTCAAACCTTATATTC
GAAAATTAACCTTTGGGAGGCTGAGGCAGGCAGATCACCTGAGGTTGGG
AGTTCGAGACCAGCCTGACCAACACGGAGAAACCCCGTCTCTACTAAAA
TACAAAATTAGCTGGGCGTTGTGCATGCCTGTAATCCCAGCTACTCGGGA
GGCTGAGGCAGGAGAATTGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAG
CCGAGATCACACCATTGCACTCCAGCCTGGGCAACAAGAGTGAACTCCA
TCTCAAAAAAAAAAAAAAAAAAAAAAATTAAACCTCTGGAAGTTGAGTTTG
CAAATATTATTATGCTCATTTTTTAACCTTGATGTTTGGAAAAATGTCATG
ATGAAAATTGAGGTTGGGGGATGAGAAAAAAGAAAAACATCAACCCAC
AGCCCATTCATTTTTAGCCCGACCCACAGCTCCGGGGAAGGCGAGCAGG
TCCATCCTTCACTCTTTCTTCCCTCTTTCCCCTCCTTCTGGCTCTTCCA
CCTCTAATTTGGAGCCCAAAAAAGGCACTGGGAAATGGAAAAGTCTTTT
GTACGTGGTACTTGCCGGGGAAGCTGCCATGAAAACCTGGCCCCACGGTG
GGGAGGGAATGCCCANCTGAGGCCTCGTGCCCATGCTAGGATAGACTCGT
CCAAACATGTGAGTGGTCTGACAGGGCAAGCANCANGAAATCATGTATG
AGTATGAATGATCTGTATGCAAGGGCGGGGAGAACACGGGAGGAATGG
GGCGTGAGAAAAACAGCACAGTACGTTTTCTTAGCAGCTGTCTCTGCTCAG
CCATGGGAGGTCACAGAGAAAGAGGCTTGAGGCGTTATTTTCACTGTGA
GATGTGAGTGTA AAAAAGTGCCCAAGACACAGTGAGTACCAGGGAGATGC
CCTCTTTCTACCCGAATGCAGAATGGCCACAGGCCTTAAACACACACA
TGGGTCTTCAGAGGAGAGAGGCCTCCACAGTGGACACCCGCATTCTCCCC
TGGTCAGCAGCAGCAGGGCGAGTGCTGGGCCATCATGAAGCTTCACAGGC
AATGAGCTCTCAGCAATAACAGGAACAGTGCCTGGGGGACTGTAGCTGCA
AGACCGATTTTCATGTAAGATGGCCTCTGAGGACTCCGAGATACACCAGG
CTGAGACTAGCTGGCAGCTCCAAGTTGTTGGTCAGAAGAGAACAGGAACT
AGGGAATTTGGAATTACTGTTACTACAATTCCTTTACATCCGCACAACCA
TGAGGTCAGCGATTCTTATTATTTTTTTTTTTTAAAGACAGGGTCTCAGT
ATGTCTGCCCAGCATAGAGTGCAATTGATGTGATCATGGTTCAGTACAGTAT
TCACGTCCCAGGCTCAAGTGACCCTCCTGCCTCAGCCTCTCAAGTGGCTG
GGACAGCAGTTGCATGCTACCAGGCCAGGCTTTTTTTTTTTTTTTTTTA
GTTTCTGTAGAGCACATAGC

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GGTTAACAAATGGCACAGGGAAACAAACAGTTCCAGGTGCAGGGGCTCTAA
ATCTATCATAAGATGTTAGGTATGGGGGCTCTGCCGGACACAACTCAAG
GCTTTATGCTGTTATCTCTTGAGCGAAATCCTGGGAACTTCGTACATTGC
TTGCTTCAGTACCTTATCAGTTAATCGGACTCTTTGATATGTTGGGAGTC
AGCGTACACAAGTTAACTCCTTGAGGAAGGGGGTGGGTAAGGAGTCCTTG
ATGTCTGGTAAATGAAGGAGCGAAATCGAGTTCCTCTGGCTTTCTCAGCT
AAGGGAGAGCTTATTCATGTGGAACAAGGCTAAGTGATTAAAGGAGAAA
GGGAGAGTCTGAAAACAAGGTTAGGTATTACAATGTCAATAAAATTGGTC
TCCTTATACAGTCTATGGTAGATTTCTTTCCATCTTTAATCTCCCTCTA
GCACCACCAGACTTTTTCTCTCTGTACCTTGAGATGTAAATTTTGCTATC
TGAATTTTCGTCTAAGAGTTGTTTTCTTTAATATGCAAATTTAGGGTTAT
TTAGCTGACAACCTGCCAAAGTAGTGAAACAAGTTATCAAGAACTTGAACG
TCTAAGGTAGGAAAAAAAAAAGTCTTTATGAATCTATAAGATGTACTTCT
ATTGGCATGCCTAATACGTCTATGTATTTACGTGTTGTGTACACAGTTTT
TCACTACTGAAAATATATAGAGGAGTTCTAATTAATTGACTTAAGACAAT
AAAAGCGCTTGAATCAAATACCTTATCAGGAAAAAGGAAAAGACAAGTCA
AATGCTTTCAAGTTTATATAACTTAAGTAAATCTTTAATAAATAAGC
TAGCTTTAACATTATTTGAAATGTCTTAAGAATTGCCAGCAGGTTCTGGG
TTACAGAACTAGTGGGGGTGCAGTGGGGTGAGGGTTGGTGGGGTGGGGGG
TGGTACGGGGGCTTTGTTTTTTCTTGCTGCCCCCTTCTGGGTGGGGGAAG
TGGCAGGACCTTGGCAGCACCCCGAGCCGGCATGGCGTTAATAATGGAGG
GATGCCAGACCCAAGTGGCTAAGGCCCGGCTGCAGAGCCAAGTTGGCATT

FIG. 4 (10 of 61)

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TCCAGACTGGGGCTCGGGCCGCACCCTCTCCAGGACCCTCCCCTTGTACC
GAGCAGATTGTGCGGGCAGTTTGGGCCAGCTGTCCTGGCGTGGAATTTTC
CCAAATTCAACAAATCCTCCAAGAAATCAATCCATCCATTATCCATCCA
TCCATCCATCCATCCATCCATCCATCCATCCGTGGCAGATTATGAAGCAT
GGATCATTACTTTTGGGATGTGGATATATTGAGTTAACAAGGAGCAGCTT
TCAAGAGCTGGATTTTATGCTTTGGGTGAAGTTTAGAAACACTAGCTCCC
AC

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ACCTCATGTGCTCTAGCGCCTCTTACCTCATGCCCTCCACTCTCAGTCTT
GCACTCACCTTGCCACACTCAAGGGCTTCCCCAGGTTCTTTCTTAGATTTC
CACCGATAGCTCAGGGACTTTGCACATGCTACGGTCTCTGCCTGGCTCCT
CCCCAGATCTTCTCATGCCTAGCTGCTTCTCATCAGCACCCCTCAGAGAC
TGTCCTTGCCCCACCTCTCCAGGTTCCATACCTGCCACCCTCCCCCAATC
ACGTAACAGTTTCTTACAGAGCGAGTTACCATCCAGTATTTCCCTAAC
TTATTTTTTGTGACTGGTCTGTTGCCTGTCTCCACCACAAGAACATAAGC
TGATGTGAACAGGAGCCTTGTCTATCTTGTACCCCAAGTGTGTGACA
TAACCTGATACACATTAGATGCTCAATGATGTTTGATGAATGAAGTGCTG
GTAGTCCAACCTGTGTTTCTTGTCTGTGTAAGTATGTCTGTTGTGGTTTC
CTAAGAACCTACAGCTCTCCCACTGTGACTCCTGTTCTATGGTCTGATT
TGCTGGAGCTAGAATCCTAACCTACATGCTTACTCTTAGTGTCTTCCCCA
GAGGCTGAATCCCAGTCCCTAAACCTCCACCAATGGCTAAGACCTAGCT
TCCAACCAGACAGGCCTACGCTGAGACCTCAGCACCGCCCTTCTGCGGTC
TCATCCTTAACGCATCCTTCAGGGCCAGCTTAAATGTCTCTTCTCCAAG
GAAGGCTATCCTCTTTCTGCCCTCAGTGCTCTCCATGCCTCCTCTATGC
CTCCATGCCTGCTTTCCAACCCTGCAGAGGTGGAGAAGTTGCTAATCTGC
TGTGTTGACATGTGCTGGGGTGCCTTGGGCCAGGGAGCAGGCTGGTGGTG
TGCTGATAGCCCGTGGCTGTGCCCAGGTCCATGCTCACTTCTGAGCCCC
AGTGGAGTAGGCTCCCTTTCCCTTATTGCAGCACTCAGAGGAAGGACGTG
CTTCTTAGGACAGATCTGGCCAACCTCTCCCTCGTGAGAGAAGGCCAGC
CATCCTCTTGCCCTCTTCTTCTCTGCCCCGAGTAATAAAGGTGCCT
GGTCAGAGCCTTCTAGAAGGAGACCCAAACATCCACCACACATTCCCAGT
TCCAACCGTCATCCACATGGCTGGCTGTGCAGGTAAACGCAGAGTCTGTT
TCACACACCCCAACCATCTAGTATTGGATGGGAGGACAGTAGCGTGACACT
CTTCTCCAGCCTTGAGCCCTACTGTGGGCCCCACCCAACCCAGATACCAG
AGGAGCCCTGTACTGGGATGCTATTGGATGCTTGTCCAGTCATGTACAAA
GTTAGCCCTTTGTTATATAGAGTTAGCTACGTACATCTTCTCTGTAGGG
AACCCAAGAGGGGAGAAGAGATATGTAGTAGGATTTAACCTGCAAATCCT
CTGCTGAGCACCGTGCATACATACAGTGGGTAGCATGTGGTAGGTGCTC
AATAACTATTGACCGATCTATTGAATACACGTAAGATCGTGACACTATCT
AAAACGNGGGGTGTGGGGGAAAAACCCCCCTTGTTTAGGAAACCCAAA
TTGGACCGTGTTGGC

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GCGCGATTGTGCTAAAGATCATGCATGCCTGATCAAACGTCCCCATATGG
CGTCTCAGAGTCAACTCCTTCCCCATCAGTGCCCTGACTTCGGCATAACA
AACCTGGCAGGTAAAGTGATTAATCGGTCTGTACAACCTGTAGCCCTTAG
CAGGAAGCACTAAGCTTCGTTTTTCAATTTATTTCTTCCCTGGAACCTGCAAG
AAATGAGGGATGCCTTCCGCCATGAAGTTTTGCTGATTGTCCACTTTGTT
CTCAAGGAGATATTCACAGTTTTTAATTTGTCTTCTCTCCTGCATGGTC
TCCAACCTGTCCAAAGAAGCCAGCTGGCTCCATCATCTGTAAAATCACC
ATTGTCACCAGAGCACTTGACTTCCTGTTGCCCTACAATCCACCTGCACT
TTATTTCTGCCACCATGATAATGTAGTGTTACTACATTTTACATTCAGC
TGTAAGAAATGTACATTTACTTTAAATCAAATTAAGTCTGCTCACT
CAGTCCCCCAGTCAGTACCAACTTATAAAAGAGAAGGTACATTTCACTCAT
CACTGAGGTTCTCTTACCACTGGAAAACCTGAGGAAGGGTCTGGAGTCCA
CAGTGGTTAACATCATTGCCTCTGTTTTTTCTCCTACTCAATGTAACCAT
CCAAGGTTACTCACAATTCACAAAAGAGGTCTTACCTCTGCTCTCAA
GACCCAGAGGGCTGGGTTCTAAACTCAAAGGCCAATGTTCCCCAATTTT
TGCATTGTTTCAACATTGGGGAAAACCTCGAGGGGATTCAAGAATGGTTAT
ATAAGTTTTGTGGAAAATGTATAATTTTTTAAATTAATAACAAAGTA
TTATGGAAAGCACTAAATATTGAATTTATATAAATATTCCAAATATTTTT

FIG. 4 (11 of 61)

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CTAAATTTTTAGTGAGAACTTGAGCTTGCTTCTGTGAGATATTTATTTT
AAAAACAGATTTGACACTTAAATGTCTAATCAAGCCTTTTAAACCATGAT
CTATCTCTTCAAATTCCTCAGATGCCACCATCAATAAGAACTTTGTTC
ACACAAGTAAGTGGTAGCAAATGGCAGGGTGTTCATTTTTTTTTTTT
CTTTTTTTGAGACGGAGTCTCGCTCTGTGCCCCAGGCTGGAGTGCAGTGG
CGCGATCTCAGCTCACTGCAAGTTCACCTGCTGGGTTCACGCCCTTCTC
CTCCCTCAGCCTCCCGAGTAGCTGGGACTACAGGCACCTGCCACCACGCC
CGGCTAATTTTTTGTATTTTTAGTAGAGACGGGGTTTCACCGTGTAGCC
AGGATGGTCTCGATCTCCTGACCTCGTGATCCGCCCCGCTCGGCCTCCCA
AAGTGCTGGGATGACAGGCGTGAGCCACCGCGCCCCCGCGTGTATTATCA
TTTTTGCCTGATGAAATTTTCTTGCCACTACTCTGGATGGTTTGATAC
ATTTAAATTGTGCTTCCAGGGTACAATTATCCTTTAAATCTATACCTCTT
TCCTTTCTTTTATTGACAAATATAATGTTACACTTTTCTGTCAATTGCAGC
CACACCACGATACACAGATCCCAACAGAGTTGTAATATTTTATTAGTTT
CAGAGTTTCAATATTTTATCACTTTCAATACTTCATGTGCAGGAGTTTAA
TTTGGTACTTCTTTACAAAATAAATGATGTGCTTCCAAGCATTTCTTTTC
AATAATTCCAATCAATGTTATTAACTGAGTAATACTAGTATCTGTTTATT
CATAAATTCACAGGAAATGCTTTTTTACTTATTAGTCTTTGGAATTCTGT
TGTTTGTATAAACATCTTTCATGATGGCTTTGTGTCTACCAATAGCACTA
TTGCCAAAAGGCACCTTTTTCTTGTTCTTTACTTCACTGGTCCGAGCC
TGGTACCAACAACCTACCACACAGACTGGGAAATGAGCAATTTTGCCACGT
GCCCTTAGCTATTAATGGTGGCACTCCATAACTAGCATCTTAAGCTCAAT
TTCATGAAAGAAATGTGTTTCTTATTTTGTACTTGCAGGCACTTTTAA
CTTGTAATCTTTTATTACACTTTTAAATTTAAACAGAGTAATAGAACCC
ATAGAAGGAATCAATACCCACGAGTCCATACTGATATAAATAAATAGTT
ACATAAATAAATGGGGGAGAAATAACAGCTCTTCTTACAGAAAAATTT
CAATTAATAAATGAAGAAGGAATTAGGGAAATACAACGTTACCATTAAGC
AACCACAGTAATAATCATTACAGGCAATATCCAAAAATAAATTCAAAGC
CAGTGGGCAAAAGTTTGAGGAGATACAGGATATTAACATAGTCTCCAAAT
AGCTCATGCTATTTATAAATTACAAAAGGAAACATAACAACCTGTATAGTG
AAGAACTCAGCAGACACCACCTTAGCCAAGTGATCAAGGTTAACGTCAC
TAGTAATAGGGCTTGTGACATACTGGACTCCAATCTGATACACTGATAA
GGACACATGACTTCTGCAGTATTCTTACCAAAAACAGAATTCTAATGTAA
TTAAGGAAAATGTGAGACAAACCTATTCTGAGAAACATTCTATAAAACAA
CTAACCAATACCTTCAAATTTGTCAAGGTCATAAAGACCAGGCGATGGTC
ACGATTTGAGGAGACTAAGGAGATACAACAACATAAATACAAATGGAA
CCATGGCATTCTTGATTGGATCTTGAAACAGAAAAAGGATATTAGGAAGA
AAAGCTGATGAAATTCTAATACATTCTGTAGTTTAAATTAATAGTATTGTA
CCAATATTAATTTCTAGATTTGATCATTATACTATGGTTAAGTTTAA
CATTAGAGGAATCTGGGAGAATGGTATATATGAACCTCACTGTTCAATTCA
ACTTTTTAGTAATCTATTATTTCAAAATAAAGTT

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GGGAGCGCGGCCACGCTGATCTCTAAAGCTTTAGACCACATTGGCTCG
AGCATGGTCATGGCCGTTTCCTG

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GACGTCTTAGCGCTATATTATAAAGAAATATTCACCTCCCTGCTGAGCTT
ACAGGGTGACCTAATGTCCAACAATATGAAATCTCTTCAATGAATTGCA
GCACGTCCATATATAACCCACATGGAAGCTGTCTCTTTCTCACCTTCG
AACTTCCCATGCCAAAGAGGGACCTCTTGGACTCAAATACATCTTAGCAA
TATAGAAGATGCTGGAGACTTGTAGGAGAAGTGGAGAGGGTTTACAGTGT
AGCCCCACAGAAAACACTTATGACCCCATCAGTCACTTGTCCCTTTTTT
CCATGCCTCAGTCTAGTCAGGAAACCACTAGATCCTGGATGGCTTCTTCT
CCCTTCCCCTCCTTTCTTCTCCTCTCCCTCCCTTGCTCCTCCTTCTC
CATCACCCACTCCTTACTTCCAACCAAACTTGACTAGCTCCAGTCTCAT
CCCTCCTTATTGAAAATATTTTACTCAGCCCTCCTCCCCCACTCCTGCC
CAATCTTTATTCCTTACCTACATCAGACTTCACCAAAAACAAAGGCCAGGA
TAATAACAGGACAAACTCTTTCAAACACATTTTAAATGACCATATTTGT
TATTTTGGTACAAATTTGAGGAGTCCCAATCCCCAGGGAAGACTAACAAGA
AGTTCTCCTAACAAAGGTGGGTCTCCCTTACTAAAAACTCCTGTAATGG
CTGAAAAGAGCATGAGGTTTTCTGCATATCATTACACATTCAATAGAACC

TCATGCAGCTGTTAAAAAAGATCTGTAGAGGCTATCTTGTGACAGAAAG
GCATTGGAGATATACTGTTAGTGACAAAAATAGGTTATAAATGAATTTTT
CCATGCATGCCTCTATATTTATAAATACACACACATAAAAGACAGGAAGG
ACAGACATTAAACATTCATAGTGCTTAAGATGATGCATAGTATAATAGTT
AGGACCATGGCCTTTGGGACAGAAACTACAGCCTCTCTCCCACTTATCA
GCCATGGGACCTTTGGGCAATTTGCTCAGCCTCAAAGCCCCCTGTTCCCTTTA
TCTGTGTGCTGGGGTGTGTGTAAGAGTTAAGTGCAATACACAGAGAGAGA
GAGAGTACCTAACATGTATTATGTGCTCAGTCAATATGCATCATAGTACT
CATTGTTACATATGTTCTTAAGTGCTTTATACGTTTTTTCCCTAAGTTGA
CCATCTGTTTTTGGCATTATGAAACATAATGATCCTAACAAATTAAAATT
AAAAACATAAAGAATATTTGCCCAAAAAAATAAAGAACATGAATTCCTC
AAGTAGCCAAGGGGCCATAGACAGAAGTAAGCCCTTGGTGGGGCTTAGTT
GAGAGAAGTCTCCAGAAGGTCTTTCGTGTGTTAAAGAAGAGGGTAACAGG
GAGGAGGTGGGGAGAGATGTTAACTGAGTCTAAATGAGCACCTGGAAGAA
GAGATGGGACAGGCCACTTCTGCCTGGACTCCCTGATTGTTAAGAAGAAT
GAAAAAGAGCAGAAGTCTTCCCTGAGCCCACTTCACTCCCTGACTTAAC
CTAGTCTTTTGGCCCTTCCCTCTCACTCATGGCTACTTTCTGTGGTCACCT
TGTGTAGAAATGGATGTGCAGCCACCTCATCTTTTCTACCTCCTTCAC
ATGTTTTAGATAAATTTAATGTAGTAGAAGACGGTTACAGCAAAAAATTAC
AAAAATCAAATATCTCTGCTATCTACTGTTGCATTTCTAACCATCCCAA
AACAGTAGCTGAAAAACAGCACTCGTGGTTCGAGCGCGGTGACTCATGCCTT
TAATTCAGATACTCCGGAGGCTGAGGCAAGAGAATCACTTGAACCCGGA
AGGTGGAGGTTGCAGTGACTCAAGATCATGCCACTGCACTCCAGCCTGGG
TGACACAGTGAGACTCCGTCTCAAAAAAAAAAAAAAAAAAAGCACTCGTG
TATTTTGTTCAGATCTGTGGTTTGGGCAGGGCAGGGCTCAATGAGGACA
TCTCGTCTCCGTTCCTCGCAGTGTGAGGAAGTGTAAGTGAAGTGGAGGGT
CACACAGAAGATGGCTCCCTCAAGTGGCCAGCAAATTTGGTGCTTACAATT
GACAGGGAGCTGTTGACCAAGGGCCCCAATTCCTCTTCTATGGCCCCCTT
CTCGGGCTGCATGGGCTTCTTTACAGAATGGCAGCTGGATTCCAAGAGCA
AGTATCAACCTACAGAAGAGTGGAGGAATATTGAAAGTTCACAGTCTC
TTAAGACGTTGGCCCAGAACTGGCAAAAGCTTCATTTCTGCCATGTTCT
ATTGATCAGTCACAGAACCTGCACCAATTCAAGAGGAGAACATATAGAGG
ACATCTCTCAATGGGATAAGTGTCAACAAATTTGCATCTATCACAATCTG
TCTTTTGGGTACAACTATTTCTATTCTCCTCATTATGCAAAATATACTCA
CAACCTCCCAGGGGTCGCAAAAGCCTCATCCATTTATGGCAAAATGTGGCC
CTTTTAATTTATATAAAATAATTTGCGGGGGCTTCTTTTATATTTTAAAC
TCCCCTGC

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GTGCAGAGAAGTGATTTAAAGCCCTTCAGAAAGAATGCTTTATTCCTCGTG
GAATTTGGTAACCTTGCTTGGGTGTGGGGAGGTTTGTGAGCTTTCTCCACT
CAAATTATCAGACCTTTCCATTTAGTGGTAGACCATTTCCCTCGTCCAG
GCCAAGGGCACATAGTACAGAGAAATAGGGAGTTGTTACCCAGGGAGAGA
ACTTGGCTCTAAACCTGTAATAGAAAGGTCAGTTCTGGTCTGGAGGGTCA
ATTTTGATCTTTGGCTCAGATCCAGGAATGGAACCAAGGCTTTTGAACA
TTTTAATGCAGGGGATTAAAAAATGATACGAGTCATTACGAATATATT
TGCTTAACATCTAAAGAGATCCCTCAAAACACTAGAAAAAATAAGAACAA
AAATCTAATAAAACAAAATTTGTAAACACATTTACCAAATTTTTTTTTT
TGGTAAAAATTCAAATGTCATAAATAAAGCTAAAGTTCCTCTTGATGACT
CGCTCCTCTGCCCTATTCCACTCCAAGTAACCACTATTATCAGTCTTGCC
AATACCCTTCAGACCTCTCTACCTCTATATACCATTAGAAGCACATGGT
TTTGCATTGAGGATGTGCAAGTGTGTTTGTGTTTACGTAAATGTTATCACTCT
GTTCTTGTTCATAATTTGCCTTTTCTCTCAATGATTTGCTTGGCTATC
TTTCTATTTTCAGTAGCATCTCCTTTCTTTTAACTTACCATTGTTTATTT
AACCTTGCTCTATCAACAGATATGTAGGTTGTTTCTAGTTGATTTTCAAT
AAGTATTTATAAACAACGCATCAGTAGATGTCCATAAATTTCTTTACGGA
AGATGGCAAGTAGTGGAATTGCTGAGCCAAAGAACATGTTTAAAAAACC
AAAAAACTAGACGCTACCAATTTTCTCTCCAAATGGCCATACCCACTT
ACCCATACAGAGATGATTTGGAATCTGGCTTCTCACAAGGTGAGATGCC
TTCACAGTTTCATTCTTCTGGCATGTCTCCCTTTTGTATCTGAGAGAG
CTGGCAGAATTGTGTCACTAAATCAAGGATAGAGGGTCAATGACAGCTC

FIG. 4 (13 of 61)

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AAGCTCACAGGCACCTCTGCTTTCTTCCAGACCACCTGCTTTCTGCCA
CCAGCTCTGTTCCATCTTATAGAATGGTTGCCACTTGGGTGTCTGCTCCG
ACAGCCATGTCATCCTTTGCACTGCAGTTATGAAGCAGACAGAGCTAGGA
GAGGGGCTTTGCCAGCCTCTGCCCTAGCTTGAGAACTTCAAAAAAGGAG
GGTATTGAAGTTGAACCCCCAAAAAGGGGTGGTCCCCACACCTCAAAA
AGTGGTGCCTCCGAAAGAAATGTAAAATTCGTGTGGGGGGGAAAAAGGT
TATTTAGAAATTGTTGGCTTGTCTGTCGCGAAAGTATGTGTGTTACGGGG
AGTACGGAAATTTTCGAGGGGTGGGGGCGAGGCCGTGTGTCTTTAGCCCG
GGGTTTTCCCGTCGCATGTTTAAGGGGGGGGAAGAGGGGGGATGTTTTCT
TTCCGCGAAGGTTTTTGAAGAACGGCGTGG
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CCCCCACCGCCACTACTCAACCGGCCGTTTACGAAACAACTCGCCACAT
CCACTAACCCGCTGGCTCACCACCCACCGCCCTCCCGATCCCCCAATCC
AAACTCAACCCCCACCACCAAGCGCCTCCCCCTCCCCACCCTCCAGCT
CAGCCCCAACCTACCACCAACCCCGACTCGCCACCGAAAACCAACAGCA
AACCCAAATGCCACAAAACCAAGTGTCAAACCTCCTTCCCATCAGTTT
GGTGGGCCCATCACCCTTCCCCTGGCCCAGGCTCTCCTTTGTGCGCTT
GGAGCAGCAGACTGATCTCCAGCCTTCACTCACTTCATGTGGTAATCTG
TTGTGTTTCATCACTGTGAGAATCTTCTGCATCCCCTCACTACTCTGCTGA
AAACACTCTAGTGGTTCTCATTGCTCATTAAATGAAAGTCTAGATATTAA
ACGTAGAAGGCCCAGCACAATTTGCCCCATGCCACCTACCTCTCTAATC
TTTTCTCCTTACTCTGACAGACTCTCCGTCTGTCAATTTATGTATTCTTTT
ATTGCTCTCTTCTACTTTTAGTATGAACTGGATTTATGGATTTTTTTAAC
ATTGCTTTCAAGTATGGAATAAAGAATTTTATTTATTTATTTATTTATTT
ATTTGAGACTGGGTCTCACTCTGTTGCCAGGCCAGAATGCAATGGTGCA
GTCATATCTCACTGTAACCTCGAATTCCTAGGCTCAAGCCATCCTCCTGC
CTCAGCCTCCTAAGTAGCTATGACTACGGGTGTGCATCACCACATCTGGC
TAATGGAATAAAATATTACAATGCCTAATCTTAATTTTCAAATTTTAA
TTACATTTGATCAATATGCCATGCATTTACTTTTTTTTCACTGGGTCAATAG
CCCTCACTTTGGCAAAGTCCCAGGCCCAAGGTAAGGCCTTACTTTTTCC
AAACTCATCTTTTGAAAGACATAAGTGCCTGTAAGTTGTACCACATTAGG
TTCTAGGAATTTTTTCAACAAAGACTTTATCAGACTATTTTCTCTAAGTT
GAGAAAGAGCTGGGGGCAGAATATGGCACTGAATGACTGAAGAGAAGGCA
CTGAAATCAGGCCAGAGGTTGCTGGAAAGAGCAATGAGGAACACCAGCAG
CAATGAGGAGCCGGTGATGATTTTGGCTTACAGGGAGGTGTGTACCACA
CCGATTTTATCTCTACGTGGATGAACCACAGCTGTCCGGCTCCCTTGTCTC
CAGGACATCACACTCTCCACATTCCCTCCCATCTTCCGGCTTCTGCTTCC
CGGGGCCCTCATCTGCCCCATCCTGGGTGAACACTGGTCCGTCAACTGCT
GGCGGTACCTTCCCGCTCTGCACACCCTCCCTGGCCACCCACCCACTCT
CACGGCTCGCATGCAGAGGAGCCGCATCTCTAGCTCCAGCCCATCTGCC
TCTTCTGAGCTCTAACTTCATGTAGGCGACTCCTGCCGGTGTGCTCAC
AGGCCCATCATACTTCAAAGCATTTTCCCTCAGAACACCATGTCTTGGC
TGCTCCCTCCAGAAGATACATCTCTCAAGCACATCCCCGCGGCTCTCACC
TGGATGACTGCATTACCTTCTCCACATTTGCCCCCTCCTTTGGATGTA
TATAGATTGTTTTAAATACAAATCTGATGTGCTTGCTCTCCTGCTTGAA
ACACCTCAAACTGCCTTCAAGATAAACCCTGCCCCCTGACATGTTTACA
GGTTGCCCATGGCCTGGCCCTGCCCATCTCTTCAGCCTCATCTCATGCCC
CTTGCCCCCTCGCTCTCTGGGCTTCTGCCTCCCTAGCCCTCCTTTAGGTTT
TCTAACACACCATAGTCCTTCTAGTGTGGGGCTCTGCAAGTGCTGTTT
CCATTGCTGAGACATGAATCCCTCTCCCTATCTCTACCTGCACCTTCAT
CTGATTAATCCCTACCCTTCCCTACTCATGATGTTGCTTTCTCAGGGACTC
TCTCTGACTTTTTAACTAATCAGGGTCTCCCCAGTATATATCTTCATAG
CACTCTGTATTACTCCTTTCTTAATGACCACCTGCTGTAGACAGAATGTT
TGTCTTCTCCAAATCATATGTAAACCTTCCACCAGAGCGATGATTAG
AGAAGCCTCCC
>Contig37
GACTGACATTCAGAAGATATTAATAAGAGCACTAATGATGGGGATTGCAA
CCATGTCTTTACTGACTTCCAGAAGCTTCTTACAGTAAACATGAAATCAC
ATAATTTCTTCCACTTTCCTACTGTTTCTTGTCTGGGCTCTGTCTGCT
TACTGTCTAATATCTTGGCCCCCTTAAAGTTGCTAATCTTCAAACCTCA

TTCTGTGACTGGGCGCTGGTCCTTG...CATGGGCCTTGAAGATAC1...
CTGTACACTTATCTGGAGCATCCAGTGCCTACCACCTGACCCAGATTTCCT
CATTGCGCTCCTCCCTCCTCCACCTAATGGGATTGTCTCATACCCGTGTG
GGACCCCTCCCATTTTCCCCAACTGAATACTTATCAAGACAACGCATTGC
CATACTCCCTCGTACCCTGCTCTGGGCATCAGACTGAATGTTTGTTCCTA
TTGAGGATCTGCAGCTGCATCAGTTTCCCCAGCACCGTCCAACCCCTTGA
GCATGGCTAGTCTTAAAGCAGAGAATTAGCCTTTCTATCCCTGCTGCTAT
ACATGCTGGGACAAATAAAGAAATGACAGCATTTTATGATAATGCAGG
CTGCAGGAGGCAGGAGGCAGGAATCAAATTCGTGCTTATCAAATAGTGCT
CCAATTCTTTGAATATTGGACTATAGAATATGTCATGGATCTATGCTCAG
GTGGGTTCCTATTACTCACTCCACTGAGGCCAGGTTGTGGGATTAGCTG
TCCAAGAGGGAGTTTCAGTCTCACAGCATAGGGTCATTCTGAGAATTACT
GGCCACACTTGTGTGGAGACCTCCAGAGAACAGAATCTGGGTGGTGCC
ATGTACTTCCAGGAGGAGAGAAGTGGCAGGATGCCAGCCCCACAATCAG
AGGGGAAGGGGCAGAGCCACATGTATGAAGATCCTCTCCCCAGTACGTGC
CAATCACAGGGCTTCCTAGCTTTTGGGCCAAGGAAACAATGTGGGAAGCA
AAAAAGGACAATTTCTCCTCCCTTTGCATGAAGACTGAGCAGTTTACC
AGATTCCCGGGGAAACACCTTCCACTCTGGGTGAATGTGAGTGAGAGA
CATTGAGCTGGAACACTAGAAAACTATTTCTGAGCCACTCACCTTTAG
CCCTAGAAAGTGTGGATTGTCTCTCATCTTTGCCACAGTAGAGACTGC
TGATAGCATCAGAACTTGGGCTCTGGAATTAGACAGATATGGGTACAAAT
CTGAGCTCTCTCACTTATTAGTGTGGGATGTAGAGCAACTTTTAAATCC
TTCCAAACCTCAGACTTCTCATGCATGATGTGAGGATTGTAATAGGGCCC
ACCTAATAGGGGTTTTTGAAGATTAAAAAGTTATTCAATGAACAGCATT
TAGCAAGATGCCTGACCATTGAGAAAATAACAAATGTTTTATTATTATG
TTATTATTAAACATCTTCTCCTGCACCTTCTGACTGGGGGCATCGTATCAT
CAGAAATACCTTAGGATGGGATGGATTCTGTCATGGGCTGAGTCAAGGGTG
CAATAATGGAGGAGTGAAGAAGGAAGAAATGGAGGCAGAAATCCCCAGGA
GCCCAGCATGGTACAAGGCTGAGCTAGTGTGTCAGAGCCCTCCTTGAACA
GCCACAGAGCTTGCATCTGGCCCTGGAGGAACCTCTTCTAGCTGGCAGGA
CCAGCCACAACAGTGGCCAGGGGATTTCCAGGGCGTGGGCTCCTCAGGA
GTTCAATTGGACCAAGCCTGCCTGGAGAGGGGTTATAACAGGGATCCTTC
CCTACTGGCAGGTGATTTACCCCTCGGTGAGAAGCTCAGGCATTTGTTTG
ATGGAAGGTGGAAGGCCCTGTGCTGGGCCAGTGACTATCAGGGATGGGCG
GGTGGCTGGAAAATAGCAATAAGACAATATGATAACACAGTTAACCACC
ACACTATGTGAAGCTACAATATGGGTATCTGTAATAGACAATTCCAATGT
AGAGAATAATTTAAGGTGTCACTCTCCCCGCCAATGCCATAAGCACACG
GCCTCTGCTGGGTTTCTCACTGTGGAATGTCTCCTGGTCTCCTCATGC
CCAGAGAGTGGGAAGTACTCCTACTTTAACACCGGCTTTCTGTCAATTC
CNTGCAGCCCTCCTCAGCCCCCTCTGCACAGGGAGGTTTCTCCTGCTG
CTGCAGTGCTTTGTACTTGTAGTGGTACCTGCACACAGGTATTGGTGTC
CTTGTCTCACCACCCTACATCACTGTAAGCTCCCCAGGAGCAGGCTTCCT
GTTTGACTCACCTGTGATCCTCCACCTCCCACCTGTAGTGCCTCAAGCA
TTCTGTAGAGCATGGACGCC

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GACTAATAAGTACTTCATTATTTGGGTATTTTCCAAGAACAACATATTGT
AGGAAACCATTCTTTCTAAAAAAAAGTGTCTTTTAAAAAGGTGAATA
ATTTTTGTCTAATTCAAAGTTTATTGAAAAGTTATGTATAAAACAAGGTA
AAAGGAACAAGGAAATAAGGGAAATGTAAAGAAAATTATAGAAATAAAGT
GGTATTTTTTGGTAAGAAAGCTTAAAGAGAAAATAATTTTAGGTAAGAAAG
AATCTTACCTAAATTTTGTGCTAGAATAAAGTGACTGGCTAAGAAAGGG
ATGTTCAAAGCTATTTATGACAAACCCACAGCCAATATCATACTGAATGG
GCAAAAGCTGGAAACATTCCCTTTGAGAAGTGGCACAAGACAAGGATGTC
CTCTCTCACCCTCCTATTCAACATAGTATCGGAAGTTCTGGCCAGGGCA
ATCAAGCAAGAGAAAGAAATAAAGGGTATTCAAATAGGAAGAGAGGAAGT
CAAATTTTCTCCGTTTGCAGATGCATGATTGCATATTTAGAAAACCCCAT
CATTTCAGCCCCAAAACCTCCTTAAGCTGATAAGCAACTTCAGCAAAGTCT
CAGGTACAAAATCAATGTGCAAAAATCACAGGCATTCTATACACCAAT
AATAGACTAACAGAGAGCCAAATCATGAGTGAAGTCCCATTCACAATTGC
TACAAAGAGAATAAAATACCTGGGAATACAACCTTACAATGGACATGAAAG

FIG. 4 (15 of 61)

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ACCTTTTCAGGGTGAAC...GCAAACCAC...CTCAAGGAAATAAGAGAG...
ACAAACAAATGGAAAAACATTCCATGCTTATGGATAGGAAGAATCAATAT
CGTGAATGGCCATACTGCCCAAGTAATTTATAGATTCAATGCTATCCC
CATCAAGCTACCATTGACTTTCTTCACAGAATTAGAAAAACTAATAGCC
AAGACAATCCTAAGCAAAAAGAACAAAGCTGGAGGCATTG...GCTACCTGA
CTTCAAACCTATACTACAAGGCTGCAGTAACCAAAACAGCATGGTACTGGT
ACCAAAACAGATATATAGACC AAAAGAACAGAACAGAGGCCTCAGATATA
ACACCACACATCTACAACCATCTGATCTTTGACAAACCTAACAAAAATAA
GCAATGGGGAAAAATAATTCCCTATTTAATAAATGATGTTGGGAAAACTGG
TTAGCCATATGCTGAAAACCTGAACTGGACCCCTTCCTTACAACTTATAC
AAAAATCAACTCAAGATGGATTAAAGATTTAAACATGGCTGGGCATGGTG
GCTCAGCCTGTAATCCCAGCACTTTGGGAGGCCGAGATGGGTGGATCAT
GAGGTCAGGAGATGGAGACCATCCTGACTAACACAGTGAAACCCCTGTCTC
TACTAAAAAATACAAAAAATTAGCTGGGCATGGTGGTGGGCGCCTGTAAT
CCCAGCTACTTGGGAAGCTAAGGCAGGAGAATGGTGTGAACCCAGGAAGT
GGAGGTTGCAGTGAGCCAAGATCACGCCACTGCACTCTAGCCTGGGCAAC
AGAGTGAGACTCCATCTCAATAAATAAATAAATATGGAACCTCTCCAACA
CAATAATAAGACAAACCCCAATGTTTTAAATGGGCAAAAAATATTGAA
CAGACACTTCACAAAAGAGGATATGTAAATGGTCAAAAAGCAGATGAAAA
GATGTTCAACACCATTTGGTCATCAGGGCAAAGAAAACTAGAACCACATG
AGATGCCTCTGTACACCACTTAAATGTCCAAATTAAAGAAAAACAAGTTTT
GGCAAAGTTGTGGAGCAACTGAAATGCTCGTGATTGCTGGTAGAAAAAC
AAAATGGCATAACCATCGCAGATAATTTGTTGTGAGTTTCTTACAAAGTT
AAACATATACTTATTGATATGACAGTTCCATTCCAAGAGAAATGAAAACA
TAAGTCCACACAAAGACTTGTACCTGGGTGTTGATGGTAGCTCTATTCTAT
AATTGCCAAAATCTGGAAACAAATCAAATGTCCATCAGCAATGGAATGGA
TATACAAATTGTGGTACACATGTACAATAGAAAACTACTCTGCAATGGAG
AGAAATTAACCATTGACAAACACAAAACATGGACAAACCTCAAAAACAT
TATGCTGAGCAAAAAGAGCCAGACACAAAAGACTGCTCAGCGCATGATTC
CATTCTATGAAATCACAGAAAGGGTCAGTTGAAGGTGCAGAGACAAAAA
GTAGATCTGCAGTTGCCTGGGGATGGGGTGGGAGGTTGACTGCTCTGACG
CGTAAGGAAATTTGGGGGTAGGTGGGGGATGGTGGGAATATTTTTTTGAAT
TGAATTGGGTAATAGTTTTTAATAGGTAAATATTGGACCCACAGTATTT
GAGATAGGTTTCAGTCAATTTAGACAGTTTATTTTGCCAAGGTTAAGGAT
GCATCCGTGACCCAGCCTCAGGAGGTCCTGACAACCTGTGCTGAAGGCAG
TCAACATACAGCTTGCTTTTATTCTATCTTAGGGAGACATAATACATCAAT
CAATGCATGTAAGGTTTACATTGGTTCAATCTGGAAAGGTGAGGGAACTT
SAAGCAGGGAGCTTCCAGGTTACAAGGTAGATTATTCTCAACAGAAAGGA
ATGCTGGGTTATGATAAGCGGTTGTGGAGACCAAGGTTTTATCTTGTAG
ATGAAGCCTCCGGGTAGCAAGCTTCAGAGGGAATAGATTGTCAAAGTTTC
CTATCAGACATAAGGTCTGTGTTGATGTTAATGCTGGTCAGCTTTTCCTG
AATTCAAAAGGGGAGAAGGGTATACTGGGGCATGTCCAACCTTCCCTTCC
ATCATGACCTGAACTAGTTTTTTTTCAGGTTAACTTTGGAATGCTCTTGGCC
AAGAAGAGGGGTCCATTCAGATGGTTGGGGGGGCTTAGAATTTTATTTTT
GGTTTACAGTGAAGACTTTTCAAGCTAGACACTTAAATGAGTATGTTGCA
AAATGGCAATTTCTTAGCACGGC

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GACGTCCTAAAGAAATGCTAAGGTAACCTCAATTAACCTATGCTAGAAAAGA
GAGTTAAGTATTTAGGAGGATTTAATATGGTGTAAAGTTGTGAAATCA
AAATGGAGACACTAATGTTAAGAAAACCTGATAATGGAGCCAGGGAAG
GCCATGAAGAAAGAGTTCTCACACTTGATCCCTGATCATGAAAAAGACT
CTGCAAAAAACAAAACCTTGACAAAAGGCCATTGCAACCTTACACAAAAA
ATACTACTTTAAAGGACATGTGCCAGCAACTGCCTGTCCAACCTCAGA
CTGGCAATATCTTTGTTATTGATCTTAGTAGCCAGCATAACTATTTCAA
AACAGTGATGTAATGCTCATTTTTTTTCTTTTGAAAACCTTTGTCTTCCT
GTAAAAACCTTTGTCTTCTTTACTTACCCTGAATATGCACAGAGTTTACT
ATGGAGTGATATTCCTGTTGCAATGCTCTATTCCCAAACAAACATCATT
TTCTTTTAGAGAGCCTCTCTCTGTTTGTGATTTAGGTTGGTGATGTAAG
CAATGGCATAACTGAACACTGATTCAAAGAAAAGTGGCCTTTTCTCTTTGT
TGTATTAAAAAGAGGCCTTATAAATAGGATAGTAAGATTTGTAAGTTGAA

CTTAAAGCATGAAGAAAATTTAGGGGCCAGGCAGGGTGGCTCACACCTGT
AATCCCAGCACTTTGGGAGGCCAAGACAGGAGGATTGCTTGAGCCCAGGA
GTTCAAGACCAGTCTGGTCAACACAGACCTCATCTTTACTAAAAATAAAA
AAATTAGGCCAGGTGCAGTGGCTCATGCCTGTAATCCCAGCACTTTGGGA
GGCCAAGGCGGGAGGATCACTTGAGGTGAGGAGTTCGTGACCAGCCTGGT
CAACACGATGAAACCCCATCTCTACTAAAAATACAAAAAATTAGCTGGG
TGTGGTGGCGGGCACCTGCAATCCCAGCTACTCGGGAGGCTTCAGGCAGG
GGAATCACTTGAACCTGGGAGGCGGACATTGCAGTGAGCTGAGATAGTCC
CACTGCACCTCCAGCCTGGGCGACTCAGCAAGACTCTGCCTCAAAAAA
AAAAAAATTAGTCAGGTGTGGTAGCACACAGCTGTGGTCCCAGCTACTC
GGGAGGCTGAGGTGGGAGGATCATCTGAGCCCAGGAGGTCAAGGCTGCGG
TAAGAGCTGAGATTGTACTACTGCATTCCAGCAGGGGCTACAAAGTGAGA
CCCTGTCTCAAAAAAGAAAAAGAAAAAGAAAAATTATGTTTTTAAATTTA
TAATTATAATAAATTTAATTACATAAATTTAAGCTCAAGTAATTGTAAAT
ATTCTTTCTGTGCACATAAGTTATTCTTGATTGACCCACAGGAGCTGG
CCATTCTTCAAGTCAGAAGGCCTGAGAGAGGAGCTGCCAGGTGGTCTTC
ATGGGGCTGTGCGGCCAGTCATCCCCACAGGTTGACAATCCTTGTGTAC
TTCATCCTCGTTGGATCCTCTGTATCCCTGACGATGAGCAACTGTGAGGC
CCGTTTCAGCACTGAGTTCAGTCAGGAAAACATCCACCCACCCACCACA
CGCTCACACATTACACACATTACACATGCACACACGTTCTGGCTCCGA
AAAAGAAAAAAGCAATTTAAATAATTCTGATCCTTTGCTTATTT
CCACAACTCCATGAAAATTGTACATTGTCCAAGCAACATTCTTAATAT
TCTCTTTTTCTCTCATATCCATTTTCTTACTGCTGTCTCCACCTTTCTC
TTCCAACTCCCTGTTAAATCCCTGCCCCAGCGAACTTTTATTCAATTT
TGTGGAATGGAGGCTGCTCTGATTTAAATTAATAAAAAAAAAAAAAATCCC
TACTCCATGTCCCAGATCCCTAGTTGTTTTTTGTTTTTTGTTTTCTGAG
ACAGGCTCTGTGTCTTCCATGCTGGAGTGCAGTGGCATGATCATGGCTC
ACTGCAGCCTCAACCTCCTGGGCTCAAGTAAATCTCTTGCGTCAGCCCTC
CCAGTAGCTGGGAGTTCAGGTATGTGCTACCATGCCTAGCTAATTTTTT
TCTTTTATTTGTAGAGACCGGTCTTGCCAGGTTGCCAGGCTGGTATA
GAACCCCTGGGCTTAAGTGATCCTCCTGCCTCGGCTTCCAAAGTGCTGG
GATTACAAGTGTGAGGCACTGCACCCAGGCTGGATCCCTGCATTTTACA
GATTTAGCATCACAAAGTCTAAACAATTAGACTGACTAAGGCAGAAGT
CCCTTATGACAGCAGACATAAGAAGGAAAAGGCCAAACACTGTGTTAAA
AATTATCCAAATGTGAGGAAAAGGCAAAGAGAGTAGGTGTGCCTTTTTAG
TGTCTAAGCTGCCTGCCAAGGGGCATCTGATGCTCTCAGGCAGGAGTCC
ACAAATTTTTTTTGTAAAAGATCAGATAGTAAATCTTTTCAGCGTGAAG
AGCATGAGGTCTCTGTCAAAATACTCAACCACCATTACAACATGAAAGC
AGCCAACAGACAACATGACAAATGAGTGTGGCTGTGTTCCAGTAAATC
TTGATTACAAAAACAGGCAAGAGGCCAGAGCTGACCCATGGGCCATAGTT
TGCTGACCCCTTCTGTAAAGGAAAGTATTTTTGTTTGACTTGCTGTTTAC
CATTGATTGAACACAAGGCTCTGTAGAGTTACTTGTTAACTTGCAAGA
TTGATGAGTGGCAAGTAATTTTTATTACCAGAATATANNATTATTCTGT
TCAGTAGATAAGATAAACCCACTGTTATATTACTGTCTTGTTTAGAATGT
GACTTTGATTCATTTTTTCACAAATTCATATTATTGCCCTAATTTGTATA
TAAGTATGCTTCTTTTAAAAATATATATTTTTTAATAAATTTGAGACAGG
GTCTCACTAGGTTGCCAGCCTTTTGCTATAATGAGAGCATAAAGTGAAT
TTCACACTTTAGCCTAGTGCATAGATGGGATTACAGGCACAAACCACTGC
ATGCAGCTAACTTTGCTTCTCATTCAGCACGTTCTATTCCNNNGNTTTT
CATATACGCGTCTCTTAATGC

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CGCATTGAGCCCAAGTTTTCTTCAGTGTTAAGGTTTTTGTACTCTGTGC
CCAAATGTCTTCCAAAAGGTTAAGTTTTTTTACCTTCTGCCAACATT
ATATGAAAGTGTCCACTTTTGTAGACTTTTACCAATGCTGACTACTTTTG
GTTTCAAAAAGCTCTCAGTAATTTTCTATTAATTACTTTTACCCTTTTT
TATTGAGGGTGTCAACTTTTTATTGTTAGCATATTCTCTCTGGGCTCCA
TTGGACGCTTGGCAGCTTTTTGGTAGTAGGTGCCTTTAGAAAAGTCCTT
CTCGTCTGGCCCTTTCTGAGCAATCTAGTGAACAGAATTGGCTCCATGC
TCAGCATTGCTTTAATACGGTTGATCCAGGGCCTAGGACTCATTCCTTCAT
TACCATCCACTTGCAATTGTCTTAAAGCAAGGCTCTATTAATTTAATTTGG

FIG. 4 (17 of 61)

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CATTTCCTGTCCCAGCTCTTAGTTTTCATTAAACAAAGGCTTTAGAAAAAC
TCCCAGTAGATGCCTATGTTGCTTCCTTTTAAAAAATTTTGGAGCTGTTT
CCCTAGCCTAACCTTTTCTTCAGGGCAGGAGTTAAGTCCCTTCTACTGCA
TTCCTGTGAAGATGGTGATTCAAGAGGCAGGGCACCTGTTGCTTTGTGAA
ACAGTCCACTCTGCAGCTGGGCAGCTCTGTTACTAGAATGTTCTCCCTTC
TGGGGAGCCCAATATTTTGTATGTCCTCTGTGAATCTCATCTGCTTATCCCA
TCFGTTTATGTCTTGAAGATGCACAGGTCTGACACCACGAGGTAGCCCT
TAGAAATTTGATGGCATTCTCTGATGTGTCCCCAACTCTTCTCCAACCACT
CCTCCCAGAGCTTGTTTCTTAAGCCCCCTTGTTGGAGCTGATTGCTTTCCTC
AAGGCAGCTCAGTTTTTCCCAGTTTGCTCCTGGTGGTCCTGAAATATGAT
TGACTCCTGAATACTCCAGGTGTGAAGGAGAGTGGGGGTGGCCTTCTAC
TTGTCTATGGCCTGGGTTTTAAGTTGCTGTCCAGTGGAGCAGAGGTGACTT
TCCCAGTGAACCTACATTTTTTCCCCTCTAAATCCTTAGCAATTTTGTCTC
CAGAGGCAAGACCTGGCCAAACCATTGTGTGTTGAGGATTGAATCAAGAAT
GATTGAGGAGATGACAGTAGTCCCCCTCATCTGAGGAGGGCGTGTCCA
AGCCCCCTCAGTGAATGCCTGAAACTGTGGATAGTACCCAACCTATATATGT
CTATGATTTTCTTATAAATTAATACATGCCTGTGACAATGTTTAATTTAT
AAATTAGGCAAGAGGGCCAGGCGCAGTGGCTCAAGCCTGTAATCCCAGCA
CTTTAGGAGGCTGAGGCCTCACCTGAGGTGAGGAGTTCGAGACCAGCCTG
ACCAACATGGAGAAACCCCGCCTCTACTAAAAATACAAAATTAGCTGGGC
ATGGTGGCAGGCGCCTGTAATCCCAGCTACTCGGGAGGCTGAGGCAGGAG
AATCACTTGAACCCGGGAGGCGGATTGCGGTGAGCTGAGATCGTCTCA
TTGCACTACAGCCTGGGCAACAAGAGTGAAACTCCGACTCAAAAAAAAAAA
AAAAAATTAGGCAAGAAAGAAATTAACAACAATAAGTAATGAAATAGA
ACAATTCTAACAATATACTATAATAAAAGTTGTATGAATGTGGTCTCTTT
CTCAAAATTACCTTTTTTTTTTGTGAGACAGGGTCTCACTTTATTGCCAGG
CTGGAGTGCAGTGGCAGGATCACAGCTTACTGCTGCCTCGACCTCCTGGG
ACCAAGTGATCCTCCCACTTTAGCCTCCTGAGTAGCTGGGACCACAGGCA
TGCACCACTGTATCTGGATAATTTGTTTATTTTTTTTTTGCAGAGAGAGG
AGGTCTCACTATGTTTCCCAGGCTGGTTTTGAATGCCTGGGCCCAAGGGA
TCCTCCTGCCTTTGGCCTCCCAAAGTATTGGGATTACAAGCGTGAGCCACC
ATGCCTGCCCCAAATTAATCTTATTGTTCTATACCCACTCTTCTTCTGT
GATGATGTGAGGTGATCCATTGCCTCCTTGATGAGATGAAGTGAGGTGAC
TGATGTGGGCATAGTGATGCAGTGTGTTAGGCTGATATTGGCCTGATGATA
TGTGAGAAGGAGGGTCATCTGCTTCGGTGATCCTGGATCATAGAGTCATG
ATGATGTCAATGGTTGGATGTCAGGAGCAGACGATGTCAATGACTAACGA
TAAGCTGGACAGGTGGGATGGTGGCACAAGATTTTATCACGCTACTCAGA
ATGGAGCACAATTTAAACTTCTGAATTGTTTATTTTTGGAATTTTTCAT
TAATATTTTGGATTGCAGTTGACTGTGGGTAAGTGAACCTGTGGAATGT
GAGACTGTGGAAGTGAAGGAGTACTGTATTATGGAAGTGAACCTCTAT
TCGGTAGGGGAACAGAATTCACATTTGTGGGGCCAGGTCTCTGCATCTG
TAGGGATCCAATTGTTTCACTTCTCGTTGTAGCAAAACTTGGCTTTGGA
ATCAGACAGATTGATGTTTGTCTATCATTCTAAATGGGTGCAGCTACACTT
TCCTCAAGAGGTAGTTCTGAAAATTTAACAAAATGTGAATTTCTTGGTAA
AAAAAAAAAACCTCAAAATATTCAGTTTCTTTCTTTTGTGTCTGATGT
ACTCCATCAAATACTGGGAAATATGTGTCTCTCATAGAAATGTCATGGAT
CTTTGTAATTCTGATTATCCACAAACCTTGGGGATTAGCTGTTTCAATGT
TCCTATTTTACAGATAAGAAAATGGAGCCTGTGGTAAGTTAAGTGAGTTA
CTCATGGCTACTTAACATAATTTTACTAGGTGATAGGCCAGAGCTAGAG
CCCAGGTACCTTCTTATCAATGCTCTGCCTTGTCTCTGTGCCTTCTGT
CTGTCTGTATGTATGTGCCTGTTGACAGTAAGGCATAGTTTAACCCAG
TAGAACTACCGTTTTGTAATGAATTCACCTTGTAATGACTGACCATTCA
AGGAACAAGTGTTTTTTCTATGCTTGACACCTGTTTTGGATGCCAAAAAG
GATACAAATGTAACCTCAGACACTCTGGGCCTCATTTTGCACCTCATTAGC
ATGTCCAAATTAAGAAAGACTGACCACACCAATATTTGGTGAGGATGTGG
AAGAACGGGAACCTTTCATACACTGCTGGTGGGGATGTAAATGGTACAAT
CCCTTTGGGTAAACAGTTTGACAGTTTCTTAAAAAGTTAGACATATATAT
TACCATATGACTCAGCCCTTCCACTTCTAGGTCTTTACCCAAGAGAAATG
AAATGCTGTGCTTTTACAAATGTCTATACAGGAATGTACATAGCAACCTT
ATTTGTCAATTGCAAAAAACAGAGACAATTCAACGTTGTCAAGAGTGAATG

GATGAGCAAGCTGTGGT...GTCTATGCA...GGTATCCTACTCAGCCAG
AAAGATATGGCTAAT
>Contig41
GACAACAAATGTCATGCATAAGATGACGATGGCCTGGGTGATTGATGCAAA
CAAGGATAAAGAAAATAATCAATTTTGTCCCCATTTTCAAAGACAGATAG
CAGCAGCAAGAGTGTAAGTCTGAGGAAAGTCATATTCCTTCCTCCTACAA
CATAGCACACACACTTACAAAAACAATACACAGACTCCTGGCCAATGGAC
TTCAAAACTGAGGAGGATCATTAAATTTAAATGTTACCGCTGCATGAAA
TCTCCCTGGGTCTGCCCTCCCTTCCCCACCCTCCTCCACTTGGGCCGGG
GCACAGCAGTGATTCTCTCACCTCTCAGAGTGAGCCAGTGTTGGCTGCAT
TGAAGGCTCCAGATATGCAAACAGGGCAGATATTCCTGGACCAGGGTGCA
CAGAGTGAGGCTCCAACGCACCCTATTAAGTGCATGAAGGATGAATGAGC
CTCTGGTATGGGCTGGGACAGAAAAAGGATTCAAGGGGCCCAAAGGGT
TTGGGTGGAACCTACCAGGAGCGGCAGTACAGACTCCTTGGGAAGGTGGC
CATGATTTAGCCACATTACCAATAGGATAATCTGGAGAATTTCTTAGCT
TGAGTTTCTGGGAGAAAGCAGATTTCTGGATTATCTGGTGACAGGTAACA
GGGCCGAGTTCATCCACAGCCACCTGCAGTGTTAGCACCTTAAGCTGAGT
TCCTTGCAACCAGGATGCTGTACGCCCAGTCAGTGTGAGACGGTTCTTGG
CTGAAGGACTGAAAAGCTTGGGTAAGTGAAGTTCACCTAAGCCTCTATCTC
TTGCTCCCGTAAGTCAGGGCTCATTGTGGCTCCTTGCAAGGCTTGACTTCA
GGGTTAACAGAGAAAATGAAGGTACAAGTGCCTTGTGAAGTCTGAAACTC
CAAACAGTCATTCTCAAAGTGCCGTCACCAAGTCTAGCACATCAGCATC
ACTGGAAGCTTGTGTTGAAATGTAAATTATCAGGTCTCCAGAGCTATGTA
TGAATTAGAAACTCTGGGAATGGGGCCCTGCAATCTATTTCAACAGGTCC
TCCAGGTGATTCTGATGCAAGTTAAAGCCTGAGAACTCTGTCTTATACA
AATGGATGTCAACTCAAGCTGCTCTTCAGAATCACCTATAGCACTTGTTT
ACCCGAATCCCTGAGAATGGAGCTTCAGGACTGCTATTTCTCAAAGTTTG
CCTGGTGATCCTGAGATGGGGTTTGGGGGACAGAGATCCAAGGTGCTACC
AGGTGTGAGGAATTGTTAGAAGGCAAACCTGGCTGTCATCTAGGGTGCTT
AAAGGGTACAGATCCTAGGATTCTGCCTCTTACAGCTGAATCAGACTTTC
CTAGAATGGGATTGCTGTCCAATGGCATGCCTCCTGGGTGACTCTGATGT
ATAGCCTGGGCTGGGAACCACAGAGGATTATCTTCCATTGACCAAGCTG
ACAAACTCGCTTAAGGCTCTGAGTTTCACACTTGATTTTCTAGCCCCGT
CCTTCCATGGATCCTGCCCCCTTCCCTCCTAATCAGGAGCACAGTCAG
TGGATGCACTAATGTGGCCTCTCCTTGGCTGCAGGGAACAGGTGGAAATG
TGGCCATAGGTGTGCAGGGCTGCCTGCCATGTATTAATAGCTACAGATTT
GAAAGATCCAAGGACAAGAGACTAGAAAAAATTTAAAACAGCCAAGCAT
TGGCCCAGTAATGGCATTTCAGAAATCCACCAAAATATTAAGATGCTTTT
TGAAAAATATCCAGAGCACTCATGTAAAAGTGCTTAATTATTAATAAAAG
CTGACATGTGTTGGGTACTTCTGTGGGTCTGGCACTAGGCTAATTATGT
TTTTAGGAGTTGACTCAAATGCTCCCTGTGATAATTATGTGAAAAATAT
AATTATTAGCTCCATGGTACAAATTAAGGAGAGGTTACATAAATAAAAG
GAATGATACTCAAATTAGTAACCAGAGCCCATGCTCTTAAACACTATGCT
ATTATTTGTGGACTCTTACATAGGTGGCAAAAGTCAAAGGCTAGATTGAC
TTCTGTCCACTTCAGCCAAGATGAAGTACAAGATTCAGATACACCCTTC
CGCATTAACAACCTTAGGAATCAGACAAAATATACAAAGCATTGTTTGTT
ACACATTGGATAACAGACAGCACTAGATAGTCTGTCTGAGAAAAGCGGT
GAAATGAGCTGAGTCTTAGAATTGCCCCAGTTTACTAAGGGGCATAGTAA
GGGCATAGCTGCAGCACAAAGAAGCAGAACCCAAAGAGACTGGCGTTCA
CCTGAGTTGAGAAAACCAAGTTGAAAATTTAGGAACACTAACACAGATAT
GTAGGCAAGAGTATCAGAGAGGAGACAGTTGTAGGGAAAAAGAGAGCTTT
ACAGAGAGACGAGAGCTCCAGAGACCCGCAGAAGATTGCCCTGACGT
CACTAGCTGAGTACCGATCATGATACATGTAAGGATATTACTCAATAT
GTGGAAAAGAACAGAAGGAATGATGTCAAAGCTCACCCAAAGACAGGAA
TCATTTATGTTTCCACCAGCCAGAGTGGAACAACCTTGTAACGCATATGG
AGTACTCAAACGAATATTTCTCAATAATAAGTTCAAATTAAGTGAAGT
AAAGCCTGCCCGCTTTGTCTGGACATGCCTAACAAAGCTTTGAGGGAAGC
CTCAAAGAATGAAACCGTGTCCAAGTAATTTAACTGTGTCCAGAAAAA
AATTCAGAACATTTAAATAAATATTAATAATATGATCAAACCCAGCAAGG
TTAAATTCAAAATGTCTGGCATCCATTAAAAAATTACCAGCCTTGAAAAAT

FIG. 4 (19 of 61)

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TGGCGGGAAAAATATTA: .ATAATGAA. .JAAAAAGCAATCAACAGAA/
AGGCCTAGAAAAGTATACATATGATAAAATTAGCAGACATTAAATGGTTAT
GATTAATTTATTTTATATGTTAAAGAAGGTAGAGAAGAGCATAAGCACAT
TAAAGAGAGACAGGAAAGTCCCAGTACTCACACAGGGCCAGGAGCAGTTT
TCACCAGTCAGGTGGGAAACTTCATATTTTCATGGAGCATTGGTAGAGTA
CACAGTGTCTTGCCTTAGTAGAGGGATAAATGCTGTTCTGTTCCCGCCTA
ACCCATCTTGAAAGAAAATCTGAAAGGATCAAACGTATTCAAGTAACCT
AATCACATCCCAGCACACAGCTCGACTAGTTATAAAAACACAAAATATTA
ATATCTAGAAACACAAAAATAATATCTAGCACCCAACAAGGTAAATTC
CAATGTCTAGCATTCAATTGAAATTTTCTAGGCCATCAAAGAAGCAGTAA
AATATGACCTATAAGGCCGGGCACATTGGCTCATGCCTGTAATCCCAGCA
CTCTGGGAGGCAAGGTGGGTGGCTCACCCGAGGTCAGGAGTTCAAGAC
CAGCCTGGTCAACATGGTGAGACCTCATCTCTACTAAAAATATAAAAAATT
AGCCCAGCATGGTGGTGGGCGCCTGTAATCCCAGCTACTCAGGAGGTTGA
GGCAGGAGAATCGCTTGAACCTGGGAGAAGGAGACCGCAGTGAGCCAAGA
TGGCACCAATGCACTGCAGCCTCATTAGAGAACATCGGGAAG
>Contig42
GAAACTAAAGGCTTATTTAAAGCGCGAGACCGTGGCGCCTTTGGACTGGA
CCCTTTCTAATGATCATTTAGTATCAGGCTATGTGGGAGTTGACCGTTTT
GCATAGCCTGAAAGCCAACAGTATCACTCCTCCTCTAGGTGTGGCAGAGA
TGTGAGAGAAGGAGACTGACAGTCTGTGGGTGTGTATGCAGTGTGGGGG
AAGCGAGGCACAGGGGACAATACTGTGGTGTAGAAAAGTAGTCTAAGGTA
GCATCAGGAAATTCATGAAACCAAAATGAATTTCTAACAGCACAAAGACA
TTATTTGTTTTTGCCTCCCTCTCATTTTTTTTTTTTTTTTGAACAGAGTC
TTGCTCTGTGCATGCATGCTCGTGTGCAGTGGTGCAATCTCGGCTCACTGC
AACCTCCACCTCCAGGGTTCAAGCAATTCTCATGCCTCAGCCTCCTGAGT
AGCTGATTACAGGTCTGCACCACCCGCGGCTAGTTTTTGTATTTTGTAG
TAGAGATGGGGTTTTGTAAATGTTGGCCAGGCTGCCCTGTCATTTTTTTT
TACTAGTGTCCAGTGGAGTTTTTAGGGGCTACATAACATGATACTGTCA
TTAATCTAATGGCTAATGAAAGGGATATGTATATGTTTTTGTGTTTAAAA
CAAACCTTCTTTGGGGTCCCTCAATAATTTTTAAGAGTATAAAGGGTCCCTG
AGATCAAAGAGTTTGAGTTCTGCTGGACTGGGACAGTGGTTGTCAACCCA
GATTGTACATTAGGGTCATCTGGGAAGCTTTAAATAGTACTGATGCCCA
ACCTTACCGCAAACCAATTAAGCCAGAATCTCTGTGGATGAGAAGTCTTC
ATTGTATCATCATCACCATGACCATCATCATTGTACCGTCACTACACCATT
ATCATCATCATCATATCATCTTCATTATCATTGTTAGTATCTCCATCACC
ATCATCAGCATCACCATTATTATCATCATCATCATCCCCACCATCATCCT
CATCGGAACCTCACCTGCATGGAGGACAATCCACTATGCATTAGGTGCTA
TGCTATTTGCTATACTCCTTATTCTCACAACGCCAGAGAGGCTGATAT
TATCTCACTTTATAACAGGAGGAATCTGGATCGGAAAAGTTAAGGTAAGC
TAATTCACAGAGCGAGAAGAGATAGAGCCAGGATTCGAAACCAGTTCTCT
GCTACATCAATGTTCCAGTCCCTTGCACTATTGAGAACCTCTTTAGTTAT
GCTTTACCCCTCCAACACCACAGTAAATTTTTCTTTTTTTAAAAAAT
TATACTTTAAGTTATAGGGTATATGTGCATAATGTGCAGGTTTGTTACAT
ATGTATACATGTGCCATGTTGGTGTGCTGCACTATTAACTCGTCATTTA
CATTAGGTATATCTTCTAATGCTATCCCTGCCGCTCTCCCCACCCCATG
ACAGGCCCTGGTGTGTGATGTTCCCCACCTGTGTCCAAGTGTCTCATT
GTTCAAGTCCCACCTATGAGTGAGAACATGTGGTGTGGTTTTCTGTCC
TTGTGATAGTTTGCTCAGAAATGATGGTTTCCAGCTTCATCCACGTCCCTA
CAAAGGATATGAACTCATCCTTTTTTATGGCTGCATAGTATTCATGGTG
TATGTGTGCCACATTTTCTTAATCCAGTCTATCATTGCTGGACATTTGGG
TTGGTTCCAAGTCTTTGCTATTGTGAATAGTGCCACAGTGAACATTCATG
TGCATGTGTCTTTATAGCAGCATGATTTATAATCCTTTGGGTATATACCC
AGTAATGGGATGGCTGGGTCAAATGGTATTTCTAGTTCTAGATCCTTGAG
GAATTGCCACACTGTCTACCACAATGGTTGAATTAGTTTATAGCCCCACC
AACAGTGTAAGCAATCCTATTTCTCCACATCCTCTCCAGCACCTGTTG
TTTCGTGACTTTTTAGTGATTGCCATTCTAACTGGCACCACAGTAAATTT
TTATAGATTTTATAAGCAAATTGTATTTACTGTGCAAGAATTGGTTTATT
TTTTAAACCATGTGTTGCAAACATACAATGGTTAATTGTGATATTTGCTC
AGTACAAGATCATCAGATCACTACACAGACTTGAGGTAATTCACCTAAA

FIG. 4 (20 of 61)

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AGCAAAGAGAACTGACCCACATTAACTGAGAAGTCTTTACTTTA: 1'
CCCTATAAACGAGCCAATATGAAGAGAAGGCCTTAATGTGGTTAACTATG
TAATTTTTTTCTGACTTTTTGAAATACTGAGAAGAGCTCATGACTCTCCC
ATCTCCTAATTCTACCTTGGTGGATTTTAGACTGACCACAACCTCATGGGT
AAATGAGGGAAGACGAATAAGAAACCTTGCTTTTTTTTCTCCTTGTTTT
TGGCTGGCTGCAGTGGCTCACACCTGTAATCTCATCACTTTGGGAGGCCA
AGGTGGGAAGATCACTTGAGCTCAGGATTTCAAAACTGGCCTGGGCAACA
TAGTGAGACCCCATCTCTAAAAAAGGCGACGG
GCGGTGCGTGCCGTGTAATCCTACCTACTCAAAAAGCCGAGGTGGAAAGAT
CACTTGAGCATGGGAGGTCAAAGCTGCAGTGAACCTTGATTGCACCACTT
CATTCAGCCTGGGTGACAAAGCAGGACGCTGCCTCAAAAAACAAAAAC
AAAACCTTAATTTTTTGGCTATTCTTTTCTGGTAAGAATGGTATAGAGAT
GGGGATGAGGATGGCTATTGTATGAGAGAGCAAAACAGGGTCCAAGCAGTG
CTCTGGGCTGTCTAAGGACCAGTAGTCAGCTTAACTTCTCAAATTTCCAG
GGAAGGAGTTCGGAGTGGTAGAATATCCTGGGTATGCCAAAGCATCACC
TTGCAAATAGCCTGTCTGAATAATTTGTTTCATTGTATGACTGGAAA
CTGGCTTTGTGTATGCCAGAGAATGGGGGCAGGAAAGAGAGATTGGTGTC
TTGAGCTCTCTGTGCCTCTGGGGCAGTGATGCTTTCTCTCATGTGGAA
GGAGAGCATGACTGAAAAGGTGCACAAATAAGGTGTCTGTGAGAGAAATT
AACCTTCCAGATACAGAGACACAACCTTCCCCAAGAGGTCTCATTTGCTC
TGCTTTTTTTCTTTTTTGGCTTTGTTCTACCATTAATAACAGAACTGA
TTATGACCTCAAAAGAGAGGAGAAAGCGACTCTCCCCACCCTAGAGCTAG
TTAACCCCATATCTTCTAGATCTCAGTTCAAGAGTCACTTCCATCCCC
AATAAAAGCCCTTGAGTGCTGAGCACCTCTCCGTCATAGCATTGTCTTA
GGGGTTTTTGTACATTTTCTTGTGTGAACTTGGGTTGACATCTGTATTT
CCGACTAGATTACAGTTTCTCAAGGGTAGGGATGTCTTGCTTGCCATTT
TCAGTTCCAGCATCTAGACAGTACCTCAAGCAAACAAGGCCGAGGGGGGT
GCGGATCACGAGGTGAGGAGTTCGAGACCAGCCTGATGAACATGGTGAAA
CCCCGTCTCTACTAAAAATATAAAATTAGCCAGGCGTGGTGGCAGGTGC
CTGTAATTCAGTACTCAGGAGTCTGAGGTAGGAGAATCGCTTGAACCC
GGGAGGTGGAGGTTGCAGTGACCTGAGATCCACTGCAGCTCCAGCTTGGGT
GACAGAGCAAGACTTCGTCTCAAAAAAAAAAAAAAAAAAGAAAGAGAAA
AGAACATCAAATGAATGAATGAGTGAGATGAATGAGTTAGCAGTGTTGGA
TTTAAGTGTGAGATTCTTCCAGCTTGACTTTTTTCTTTGGCTTAGTGAT
TTTGAGGTCNCAAGATTTATTTTCTTTTCAAAAGGTGATCACTACCATA
AGATCTTCAGAAAAAGAAATGTGGCAAGCCANGTCTCACTAATGCAAATCT
CTATAACAACCTGTATCAGTACT

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GAGGTGTCTATAAATATGGACCGATAGATGAATACAGGTAGGATGGGACAC
AATCTAAGATCCAGGGGGGGGAGACCACACGCTTGGTTAGGGAGACCCA
AAGTGGACCGTGTGGCCAGAAGAGTCCCGCACTGCAGTCTAGTGACAGTG
CAGAAAGTCACTGTGGGAAATCTAGAAGTTTCTACAGGTTGCTATTTTCAT
CATAGCACTGTGCAGGCCAACCTTCTGCTCCACTGGCTGTTGGGAAAA
GCTTTCTCTTTTCTTCTAGCCAGGGAGCTCTCAAAGTGTTCCACTCTCT
CACCTCCACCCAGGCGTCCAGGTGTGGAGGACACTTGCCGGCTGCTTGTC
TGCTGACTCATCCCTTGGTTTCACTTGAAAACCTACCACCAGCTGGCCT
CTTTCCAAGCATCAGCCTCCTCATTTTCTTAATCCCTTAGGTGTGATCTC
ACCTCCACACAGTAGATTGCCTCAAGGCCCAATCCAATATGAATAAAAA
TGATTATTTTGTGATCTTCCAATCTTCTTTTAAAAATATTATTTTATAAT
TCCCTTTAGGAGGATCACCTAAGTGAAGACTATTTTACCTAAGAAATGT
TAAATGTAAAGACATGGTTGTAATCTGGGGATTCTGTAAATGGCTA
GCAGACAGAAGTCAGACGACAGGCTAGAAATGTGTGAAGAGTGGTTGCCT
TTGAAAGGCGGAGTTGGTAATGATTTTCTTCCATTTTCCATGCTTTCCA
ATTCTCTACAAAGGCCTTAATATTACTTCGATAACCAGGACCTCTGATAA
CCTGCCCCCACCAGTAAGACTTAGCTGGGAAAGTCAGCTTCATGTGAG
GTAAAGGAACCAGGTAATACACAATCCCCTGCCAACCTGTGCGGTGTG
CAGGCTGAGCTTCTGTCATGTGGGAGGAAAGAGAAAGAAGAGAGAACT
CCAAGATCCAAGAGATCCAGCAAGAAGGCTGGAGTCTGAGGACGCAGAAA
GCTGAATGGCACAGTTACCCTATTGTGCTGAGGTTCTGTGGCCTCTGGG
TCTCTTGACAACCTGGGCAAAGACCCACAGAAAACCTATCTCTAGACCCTAC

FIG. 4 (21 of 61)

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CTGTGGGAGGGGAAAAGTCTTCAGATCACTACAGGACAGCCACCTGGAA
CTCAAATGGGCTTACAGTTCCCTTCATCCAGAGGGTCTTCATCTAGTACATA
CCAGGTGCTAAGCCTGGGTGCTGGAGACATGACGGGGAACCCATTTACCA
TGGCTTTGTTACTGTGACATTACATCTAGGGAAAGCCAGCAAAGGGGAG
GGATCGAGGAGAGCTTGTAGGCAGAGAAAATACCCAAGGGCAAGGGAGA
AGCCAGCCTGTTCTGAGCACACACAGTGGTTCATCTAACTGGGCCTCAG
TGCCAGGTGGACTGGAGATGGGGCTGAGGAGCTGTACAGAGCATTCTG
GACACAGATGTACATAGTCCCTTGAGGTTAGGGTCTTAGGCATGGCAG
CATTGCTTTGAGTTTTTCTTTTGTAAATGTTGCCATTATGACAATGTGG
AAGATGGGTCTTGCAGAGAAGGGCAGGGCTGTGAGACCAGTTAGGAGAC
TAAGATGTGAGCCAAGGAAAATGAGGAACACCTGAACACTGGGGCAGGTG
CAGGGCCCAGAGAGAAGCAGATGGCTTCCTGAGGTTTTAAGTAGGTAGAA
TCAAGGCAGCTGGTAAAGATCTTTTATTACATATAAACTGGAATAAGCCA
TCTGCTCCAAGACAAAAGAGTAGGCGGAAAACAATACAAGACAGAAATGG
AATTAGAACAAACCTGGGAGGAATGTGGAATTAGAGTAGAGAGTCCAACA
CTGGCTGCAATCATAAAAATGTAAAACAAACAAAAATTTGCTAGGTGTGC
TTACTTAGAAATAATTAGCTGTCAATTAAGTTCACCTGTGTATGGCTT
AAATGTGTCCCCAAAATGTGATGTGTTGGAACTTGATCCCCAATGCAA
CAGAGTTGAGAGATGGGACCTTTAAAAGGTGATTAGGTCATAAGGGTCT
GCCCTCATAAATGAATTAATACTGTTATCATGAGAGTAGATTCCCTGATAA
AAGGATGATCTCTGCCTCCTCCCCACAGCCCTCTGTGTCATGCTTTCCTG
CCTTTCACCTTCTGCTATGGGATGACACAGCAAGAAGGCCCTCACCAGA
TGCAGCTCCTTGATCTTGGACTTTCAGCCTCCAGAACTGTAAGCCAAAC
AAATTTCTGTTTATTATAAAATTACCCAGTCTCAGGTATTCTGTTCTAGAA
GCACAAAATGGACATAAGATCATTAGATTATCATTTTTTATCAGACTGTTG
AAGTGA AAAAATAAAAATCAAATAAAGAAATTAAGAGAGCTGCATGCAGCA
GCTCATGCCTATAATCCCAGCACTTTGGGAGGCCAAGGCAGGTGGATTGC
CTGAGCTCAGGAGTTTCAGACCAGCCTGGGCAACACGGTGAAACCTGTT
TCTACTAAAATACAAAAAACTAGGCCGGGCGCGGTGGCTCACGTCTGTAA
TCCCAGCACTTTGGGAGGCCGAGGCGGGTGGATCATGAGGTCAGGAGATC
GAGACCATCCTGGCTAACAAGGTGAAACCCCGTCTCTACTAAAAATACAA
AAAAAATTAGCCGGGCGCGGTGGCGGGCGCCTGTAGTCCCAGCTACTCGG
GAGGCTGAGGCAGGAGAATGGCGTGAAACCCGGGAAGCGGAGCTTGCAGT
GAGCCGAGATTGCGCCACTGCAGTCCGCAGTCCCGCCTGGGCGACAGAGC
GAGACTCCGTCTCAAAAAAAAAAAAAAAAACTAGCCAGGCATGGTGGTGT
GTGCCCTATAGTCCAGCTACTTGGGAGGCTGAGGCAGGAGAATTGCTTGA
ACCCAGGAGGTGGAGGTTGCAGTGAGCTGAGATCATACCACTGCACTCCA
ATCCAGCCTGGGTGACAAAGCAAGACTACATTTCAAAAAAAAAAAGAAAG
AAAAAGAAAAAAGAAAAAGAAATTAAGAGAAGGGCAGGTATTAA
CCCCAAATATCCCACCATAGGGACACATTAAAGTTTGCTTGGCCACTCCC
CTAGCATAATATATGGAATGTCTTCAAGGACCCTCTGTTGTAAATACAAG
GCCCTGTCTGGACTTAATACAACCTGCAGGCTTTGAGATCCCTACTCTGTT
GCCATCTCTCATAGGATTTGCAGACCAAATCCAATACTTAAAAATAGCAA
CACTCACAAACATGCAATCAGAGCAGAAAAGAACTTCTAAAAGGCCCT
GAAACTACACTTTATGAGAGAAGACAATAGGGACCTGAGGGTGGTAGAAT
TTTCTCTCTATGCATCTATGTTTCCAGGGCTCACTTTCTCAATAAACTCT
TAAATTGCTTTTAAAGTAAGGGAACAAGCAACATTACATTTAAGAGAAA
TCAATTTCATAAAGAAGGGGGGATGTCCAGGGTACTTTGCTTCCATGTTT
TGCTTCCATGAATTTGTGTTTAAACAGAAGATGCAGAAAAACACACAATTA
TTGCAAAATCAAGGAAATCCACTCTAAACATCCCTTGGTTTCCCAGGCCA
GTGTCACAACTGAAAACACATATTGTGGCTAATTATGTGTCACAAATTAG
AATGACAAGGCAAGAAAAAAAACCTCTCTGATTAACTAATAGCAGCCAA
CACAGACAGCCTGTGTAGCTCGACTCTGCTGGTTTATAAAAGGCAGAAGA
AGCAAACGGCTTCTGTGACCGCAACAGGAAGGGCCTCTGCTCTTAATAAA
TAAATAACATTTAAATTATTCTCCCCATTTGCAAAGCATTTTCCAATC
ATTATCTCATCTGACCAGGTATTATTGTATCTGACCAAGAACTTGTATAC
NAAATAAGAATAAAAAATAATATGGGCCANGCACAGTGGCTCATGCTT
GTAATCCCANCACTTTGGGAGGCCAGGCGGGTGGATCACTTGAGGTGAG
TAGTTTGAGACCAGTCTGGCCGACATGGCGAAACCCCGTCTCTACTAAAA
ATACAAAAATTAGCCCGGCATGGTGGCACATGCCTGTAATCCCACTACT

TGGGAGGCTGAGGCACGAJAATTGCTTGAACCTCGAGAGGCGGAGGTTGCA
 GTGAGCCGAGACTGCGGCCATTGCCCTCCAGCCTGGGCGATGAGAGCGAA
 ACTTCATCGAAAAACAAAAACAAAAACAAAAACACCTTAGAAGA
 AGCGTTCCTCCTCTTGCTTTCTGAAGACACTCTACGCTGAAACAGTAACT
 TTCAATAAACCATCTCTTCTCACCGCACTCTGCGACTTGCTTGAATTCC
 TTTGTGTGCAAGATCCAATAAGCCTCTCTTGCGGTCTGGATGAGAACCCT
 TTFTTTGGAATACTCTGACACAACAAATTGCAGAAAGAAAGTCTCACATG
 TATAAAATAAGCAAAAAGATTCTCTGGCATCTGAAGAAACAATTTCTTG
 TCAATATTAGTATCACTATAAGTGTAGAACAACCTGTTGTATGATGCTAC
 ATAAAGTATATGAATCTGAATACTGTTGGATACAAAGGGAGACTATNNA
 TGTAATACGTGCGCCGAAATGACTACACTGTTGGTGATCTTTCTTTCAAG
 AAGCANAAATATTGCCTCNAACATCCTGTACATGGTATAAAATTTTA

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CCCAGCAAGAACACCAATACAACGGGGGGGGCGTTCTTTGTGAGGGGTGG
 GGAGGTCAATTTTTTGAACCTGCAGCAGGTAACACACAAAACCTCCACA
 GCTGCTACCAGCTTTCAGGAGAGCCTGTGTACCTGGAGAGGAGAAGGCA
 AGTGCTTCCGAACCTGACTTGATGTCTTAGATTCTGCAATGCGTAGTCTG
 TAGGGACAGGCTGTAGCTTATCCTATAGGCTTGGGCTGGAGTCAGCAAGC
 ATCTGGGCTGGCAGAAGATAAAAGATGCAAAGGTGGAGGAAAGCATACGT
 GGTCTGGAAGACAGACTTGGTGGGTGGGTGGCTGCTACAACACCCTAGTT
 AGAGGTAGAGGGGTAAAGTCAGTGTGTCTTCTGCACAGGCCTCTTCCCCAC
 CTCATTCTTCATTTCCTATACAGCCTTGCTGAGTTATTACAAACATCTG
 ATCAACTGGAAGCTGGGTTGAGGATGACCTAAAGGACTAGTGTGATGCC
 TGCCCAGGGGTGTGGGCCCATAGTCAGAGTCCAGAGCCTCCTCTCAGCTT
 TTAGCACATCTCACCCACATCCTGGGTCCTTAATTAGCAATATGAAAGCA
 AGCCAAGTGACAAGATTTTGTCCCTGGGAAGTCCAGAAGCACTCCTTTTC
 TCATTTGTATAAGCATAATGATTTGCTTACATAAATAATCATGAAAATTC
 AAATCCCTCTCAGAAATCAGGTCAAAAACCATGAAATGCAGCATGTGGG
 CAAGAATCACAGGGGAAAGGTAGGTCTTGGAAAAGAAAGGATGGCAGGGGAG
 GAAGAAAGCAGGGTGCCAGGGGGCCTGGGCTGCTGTCCAAGTCAGGTGGC
 TCACCGTCTCTGAGAACATTTCACTTTCTGGTAAATGGGGCAGTTGGAGA
 TAGAAGGGTTGGGTGAATGCCAAGAGTGAGCACAGCTGAGGTCAGTGCTG
 TGCTTGCACTCCAGGCGGGAGTAGAAATCCTGGGCCCATCTTACCTCCGA
 CCTCATTTCTCTCTGTATAATGTGGGGGTGGGGGAAAGTTCTGGTCA
 TCAGCCCTAGCATTCATGGTTCAATTCCTCATCAGTGATGGAAAATCAC
 CAAGCAAGAGAACAGGATGGAGAATAACCGGATGGGTGCAATCGGAGGTG
 CTATTTTCAGGTGAGGTGGCCAGGGAAGGCCCTCTGAAAGGTGGCTTGAG
 CAGGTGGCTGAAGTACAGAAGCTGCCAATCATGAAAGATCTGGGGTACA
 GCATGCCAAGCAGAGGAAATGCGAGTGCAAAGGCCCGGAGATTGGATGTG
 GGCTTAGCACAAATGTGGCATGGCAAGAAGGCCAGTGTGGCTGAAGCAGC
 ATGAACAATGGGTGGAGGGGCTGAGAGGACAGAGGAGCAGGAAAGAGCCA
 GGCTTGGGTAGGAGAGGTGTCAACTTGATATATGATGCAAAGCCCTTGGA
 GGTTCCCAAACACAAAAGCAATGATCTAATATATGGTTTTAAAAATGCCA
 CTCTTGGCCGGGCGCGGTGGCTCACGCCTGTAATCCAGCACTTTGGGAG
 GCCGAGGCGGGTGATCATGAGGTGAGGATCGAGACCATCTGGCTAA
 CAAGGTGAAACCCCGTCTCTACTAAAAATACAAAAATTAGCCGGGCGCG
 GTGGCGGGCGCCTGTAGTCCCAGCTACTCGGGAGGCTGAGGCAGGAGAAT
 GCGGTGAACCCGGGAGGCGGAGCTTGCAGTGAGCCGAGATTGCGCCACTG
 CAGTCCGCACTCCGGCCTGGGCGACAGAGCGAGACTCCGTCTCAAAAAAA
 AAAAAAAAAAAAAATGCCACTCTTGCTGTGAAAAATTGACCCTGGGGGA
 AGGAGGAGTAGAAATGTCAAAGTGGAAGCAGACCACTCAGGAGGTCAGG
 GCAATGGACTGTGCAGGAGAGACTGACATCTTAGACTCGGGCAATAGGAG
 AGAAGGTGGTGAGGATTATATTCTGGGCATAAAGGCAACAGAACTAGCTG
 ATGGCGTCAACGTAGGAGATGAGGGAAAGAAAGAAATCAAAGGGCATTCA
 TAGGTTTGAGGGTTGAGTAACTGGGGATATTTAACAGAAATGGAGAAGTC
 TGGGGAAGGGGCAAGTATTGTGGGGGAGGGGTCAAAGTTCTGTATTTT
 GGCCAAGTTAATTAATTTGAGATACCTCTTAGGTGTCCAAGTGAAGAT
 GTCAAACAGTCAATTGAATACAAATCTGAATCTTAGCCAGGATGGTCT
 CACACCTGTAATCCAGCACTTTGGGAGGCTGAGGTGAGAGGATCACTTG
 AGGCCAGGAGTTTGTGATCAGCCTGGGCAATAGAGCAAGACCTGTCTCC

FIG. 4 (23 of 61)

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ACACACACACACACACA. AAAAAGTCA1CAGGCATGGTGGCACATGCCCT
GTAGTCCCAGCTACTCAGGAAGCTGAGGCAGGAGGATCACTTGAGCCCAT
GGTTCAAGGCTGCAGTGAGACTATAATCACATCACTCAATACTACACTCCA
GCCTGGATGACAGAGAGAGACCTCATTATTAATAAATAAAATTTAAAAA
TTAATTAATAAATAAATCCAAATCTTTCCTGAGATTCATATTCAGGAGTAA
CTGTTCATGTAGAAGGCATATAATGCCATGGGTCCACATGATACCATCTAAT
GAATGCCACTGGAAAAGAGAGAATAGCTAAAACTGAGCACTGGGCACAC
CAGCACAGTGAGGTTGGAAGGAAGAAATGGAGCTAACAAAGGAGACAAAA
GAGGAGTAGCCAGTGAGAAGAGAGAAACATCTGGAGAGAAGAGAGAGCAG
CAAAAGGTGGGTGAAGGAGAATGTGGTCCACCAGGCCCAACAATGCTGAG
CAGTTGAGTAAGTGAGGACCTGGCCACTGAATTTGGCAAGAAAAGAGGATG
TCAGCGGCCCTAGAACAAAAGTGAAGAAGAGCTTGAGGACGGAAGCCTGA
CAGGAGTGAACTGAGGAGAGAATGAAAGGTGGAGACATGGAGCCAAGGAG
CACTGAGTACTCCCTTGAGTAGTTTTGCTGTAAAAATAAAAGTGAGTGCAGA
GACGGGGCAGGGGGACAGAAATGCAGGGGTAGCTGGAGGGAGCCACAG
AATCAAAAGAGGGTTTTTTGTGTTTAAGATGGTAGTTGTACATAGCACAT
TAGTAAGTTCATGTGAATCACACGTCAGGTGAGACAGATCACTAATGCAG
GAGTCAAATCCTTGACAGAGCCCCCAGAGGAGGTGATGAAGGGAAGTGATG
GACATCATTGAGATGCAAGTAGGTTAGCAATTCCTGGGGTACAAATAGGA
GGTGACTCCTTTCTGATTGCTCCTGTTTTCTGAATGAGATAGCACATAAA
GTCCACTCAGCCATGTTAGCTGTTGAAGTCCTTGTTGGCTGTCATGCCTGT
ACAGACTGGGCTCTCCTCTCCAGCATTTCTCTCAGACTAAGCTGAGCTG
CACTAGCCGCTGCCACATCCTCTTGGGGCCATCCTCTGCCACACTCCACA
TATTGCTGTGGTTTGCTTGCAACCCCTGGAAGGTCCTACTGGCTGCTCCT
AGAAGAGTCTGGGCGGCATCTCTCCCTTACTCGTTATCACATGGTGCTGT
AAGCAGTGGCCACACACTTTAGCTGGTGGGATGGGCCATCACAGGCAGTA
AATGCGAAAGACTGCTCAGATTTTAAAGCACCCATGAATCAGTAGAATGA
GTTTAGAATTGTAGTCATCAACACACATTAAAAAAGAGGACAGGCAC
TAAAAAATTAGTTGAGTAGGATAAAGCCATAAAAGATATTAATACTACAAC
CCAGATAGGAGGTGCAAAATTGTCCTTACATAAATCAGATGGAAAAAGTT
GAAAGCAGATAAGATAAAATAGGTAAGCATGACATTTAAAAGGTATTTCAT
GGGACGTGGTTACAAAACCAACTCACACTAAAAAGTCTTAGGACCTCTC
GCTGACTTAGGAGCCTGATCCCACTTTGAGAATGACTCAGTGTTTACC
CTGTGGCTAGTGATAGACCAATGATCCTGTCTCAGAGTCACTAGCCAACAG
CCCATATCAAGTAATTGAAACTTTGACTCAGAAACCTCAGTGTCAGAACC
TTTGACTTAGGAACCACTGTAGTGGTTAACTGCAATTTGCACCCCTTAG
TTTCAAGGCTTTACAACACCGGGGGGAGGGGGAAGGCATAGAGCTGA
TGACCTAAAGGAAACCCATTGCAGCAACGCTTTTGTGTTAAGTTTACAAA
TAAGTGTTGTTTTAGAATCCTCCAGGTAATGCCTTTGTTATTTAATGTGT
CTGAGACAATTCTGCACATTAAAGAATATAAAATATTACCTTGTAATTCC
AATTTGAAATGTGTAATTGACATTAGACTTCTATTTTAATTTGAAATGTC
TAAACAATGTGGTTAAGTTTGTAAAAGGTGTGTGAATTTTGAGTCTGAT
TTACTACATTTTTTTTTTAATTTTCTTTTTTTTGGAGTTTTTAGGGATTGC
TTAGATGGCTAGAAAGATCGCTAGGCACATGTCC

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GATGTGTGTACGTGTGTGCAAATACCGTGCCCTTTTTTGTGTTTCTTTTGT
GAAACAGAGTCTCACTCTGTGCGCCAGGCTAGAATGTAGTGCGGTGATGT
CAGCTCACTGCAACCTCCGCTCCAGGTTCCAGTGATTCTCCGCTCA
GCCTCCCAAGTAAGTGGGATTACAGGCGCCCAACACGCCCAGCTAAT
TTTTGTATTTTGTAGAGACGGGGTTTACCATGTTGGCCAGGCTGGTC
TCTAACTCCTGACCTCGAGATCCACCCACCTCGACCTCCCAAAGTGCTGG
GATTACAGGCATGAGCCACCATGCCTGGCCAATACTGTGCCATTTTATTA
TCAGGGACTTGAGCATCCATGGATTTTGGCATCCATAGGGGTCCTGTAAC
CAATACTGCACAAATACCAAGGGACAACCTGTATTCTAAAAAGACCAAAAA
TTAATAAGCAGGACGCTGAAGGTAATTGCCCAATAAAGTCATGATCCCT
TGCCCAAGTGTCTGAACCTCAGCCAGTTTTCATACTCAGGACCTATTGGCT
GCAGAGGTGGTAGGAACCATATGAGAATCCTGCAATATCATGGCAAGTAT
GCACTTTAATGATATCTGCAGTCCTTCCCCAAAAGGACCTTACATTTACC
ATACTGTAATGTCCTGCGTGAGAGGGTAATACTCAGATTTTTTTTTTTTT
TTTTTTTACACAACGTCTTACTGTGTTGCCACACTGGAGTGCACTGGCT

CGATCTTAGCTCACTGC .CTTCTGTTT .TGGGCTCAAGTGATTCTC
GCCTCAGTTTCCTGAGTAGCTGGGATTACAGGCGCCCGCCACCATGCCTG
GCTAATTTTTGTATTTTAGTAGAGACGGAGTTTGGCCATGTTGGCCAGG
CTGGTCTTGAACCTCTGACCTCATGTGATCCGCTGGCCTCCCAAAGTGCT
GAGATTCCAGCGTGCGCGGCCATACCCGCGCGGAATTCTTTATATATTC
TGAAAACTAATCCTTTGTGAGACATAAGTGTGTAAATATTGTATCCAG
TTTGTGGCATGTATTTTAAATTTTAAATGGTGTCTCTCAATGAAAAAAGC
TTAACTTTAAATGAGGTCAAATTGATCACCTTTTATTTATGGTTGATT
CCTTTGGTGTATGTGTAAGGAATGTTGTTCTTCTCTGTCCTCCAAAGTTGC
AAAGATTTCTTGTGTATTTTGTCTTAAAGTTTAAAGTTTGTCTTTCC
CATCTGTGCACATTTACATTTGCTACATCTCACTGACTGCTTCTCTGCTG
TGCAGCAAGCTCCATGAGAGCAGGAGGCATGGGTCTGCTTCTTGTGTG
GTCCCCAGAGCCCTATGTCTAGTAGGACCTGGCAGGGGACTAGTGAGT
AGCTCCTGACTAACTGACTCAATGAATGAATGATTGGATGATTGAACAA
GTGGTATGGGAGTTCACAGCGAGTAAGAGATGCCTTAGAAGAGATGAAGA
AGGAGATGGTATAGGGTAGTGGTCTCAATTCTGGGTCCATGGTGGACTC
ACCTGGGGACCTTAAATGTACCGTGGAGGATCCCAGCCCAAGAGATTC
TGTATGACTGGTCTAAGATGTGGTCTGGGCACCAGGTGATCCCAGTGTGC
AGCCAGGCCTGAGGCCACTGGATTTGGTGGTAAATGAGGTAACATCAAG
GGTACAGACGTTGGTTGCCAACAGGCTTGGGCTTGAATTTAAGCTTTGTC
ACTGACTTGTCTGTCTCTCTGCACTCGTTGAGCCTGTTTTCTCAGCTGA
GAGATGGGTGTGATAACACCTACCTGCTGTAGTTGTTGTGAGAGTTAGAG
GAGATAAGCATGTTCTTGAATGAAGTGTGTTCTTAATCCATCATAGGTT
TTTTGCTTGTGTTGTTTGTGTTTGTGTTTCTTTTCAAGAATGA
GGTTGAGCCAGACTTTGACAGCTGGGTGGGAAGTGAACATGTGGTGATTG
GGAGAGAAGGGCAGTTTATGTGAAGGGAATGTAATAATTAGAGAGTGGGC
GTGGGAAGACATGCTGGGGAGAGTGAGCAGGCCGGTTAGCCCTGGTAGAG
GGTGCAAGAGAGCAGTGCGGAATCTGCCAGGGAGACAGGTGGGTGACCAG
GGTGCCAAGGGTGTGGCTTTTCCCAGGTTCCCATGGACACAGCCATCCTC
CCAGATGCCCAGCCTAGCTGTGAGTGAGCAAGAGTTCTGGATTGTCTCTC
TCACTCTGTCTTTTCTCTCATTCCAGAAACAAAGCAGTGACTGGTACTT
AGGAGGAGAATCAGGTCAAGTTGGGAGAACTTGCTTCTGCTCAGGGGAG
CAGAAGCAAGAATGGAGGCCCCACCCATGCTGGAAGATGATGAGGGTTTT
GGTTCAGGGAGGAGGAATATTGGGGATCTAAAGGGGCTGGGAGTGGGGC
AGGACCCTGCCTTAGGACAGGTAGAAACATTTCTATAAAAAATGGGGTG
GAGGTTGATGGTAGGACCAGGCATCTTAGTTGGCTCCCTGGAGTGTCAA
GCCCTTGAGATGGTCTTTAAAGCCATGCAGTGGGGTTTGAATCTGGTGT
TCAAGCTCATAGGTTATTAACATAATGACACTTGAAACTATTTGGGAGA
GCTCAAGTGAGTGGCCTGGAAGTTCTGTGTTGGTGCAGGAGGTGACTTAG
GATGTGCTGCTCCAGACTCATATCTTTGACTGCACACCTGATGCTTCATC
TGGCTATCCTGTAAGCACCTTCAACTTAACATGTCTACACAGAACTCTT
GATATTCTGTTCTCTCCCCAGTTCTCTCAGTTCTTACCAAATGTTCTTCC
AGTTACCCAATTGCTCAAGTAAAAAATCTAAGTCTTCTCTTGGATTCTC
GCCTGTTCCCTCAACATCCCACCTATCCATGAGTGTCTGTGGGCCCTGC
CTCTGAAATAAATCCTGCCTTTGTCTCCAGTTCACTCCAGCCACCCATC
CTGGGGCTGCACCCTCCTCCTTCCAAGCCCTCTCCCTTTCTTCTGGTG
CTGCCTGTATGTCAAGCATATGCATCAGTGGACCAGGACATTTGAAAT
GCAACCAGTACAATTGGGCGCGGTTATGCCTACCAGTTTTTCTTCTTAA
ACATTTTATATTTATGTTTGAAAGCATGCCACCTTTCTTCACTTGCCAAC
TTGACAGATTTATTAGTTGACAACATCCGCTGATAGCATCAGTAATAAGT
TAATTGTTTTTGCACATGTAGCTTTAATTATTCTCATTATCATTATAGG
AGTTATTCTTTGTAAAGGGTAACTGAGTTTTCCAAAACAAACAGAAATTT
GGGGTGGGCCCATGGAGCGTGACTCATGAAATCAGATTCTTAGAAGGACC
TCGGCAAGTCTCTGGGTTGCTGTTAATGAGCCTGGCTGGCTGCCAGGGGT
GTGTCTGCCCTTTATGAGGCCACCACTGTTCAAATGCTTGCCTGCAGCAT
TACTTGCCTAGGTAGTGCTTGTCTTACTGAACTGTCAGGGATCCAATTC
TTTGTGGTCTAAGTAACAATACTCAGATTACAAGGAATTGATTAATAAG
CCAGAATGCCAATGTATTACATTTTTGATGAAGACCATATTTACAGTGAT
TGTATCTGCTCAAGCTCAAATTAGGATTAGAGTTCTGACAAATACATATG
TGAGAAGTATGAGGTTAAATACTTGAAATTTGGACTTTTCTAGAAAATCT

FIG. 4 (25 of 61)

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GAATGTGATTGCCATTACATACCTTTCTGGGGATGATGATTCTTGTACT
TTTATTTTAAAGACATAGAAAATACTTAAGAATCAGATTGCTTGGCT
GGGCACAGTGGCTCATGCCTGTAATGCCAGCACTTTGGGAGGCCAAGGTG
AGTGGATTGCTTGAGCTCAGGAGTTTGAGATCAGCCTGGGCAACATGGTG
AAATCCCATCTCTACCAAAAATACAAAAAACAACCAAAA
AGAATAAATTAGCTAGGTGTGATGGTGCGTGCTTGTAGTTCCAGCTACTT
GGGAGGATGAGGTGGAAGAATTGCTTGAGCCCAGGAGGTGGAGGTTTCAG
TGAGCTGGGGTTGCAACAGTGTACTCCAGCCTGGGCGATAGAGTGAGACT
CCGTCTCAAAAAAATAATCAGATTGCTTTATTGCTGGTTTTCTTTCT
AAAATGAGATTGGGTCCCATCATCCCCTGGCCCCCATTTGGTTAATGGTT
CCTCCTTTGTCTATTGAATAAAATACAGATGTCTGCTTTTGGCAACATGG
TTGAATGTAGACACTGCAGGGTCTTCTGACTCAAAATGATTTAGGCTTA
GATAAACACATTTGGAAATGCATTTCTGGATTAAACACCAAGGAAAGGAG
ATCTCTTTAAATCCCCTTTCTGTTCCCCCTCCCTACCCCCTCCAATTGG
GCTTAAGTAAGAAGGGTGGTTACCCGCTAGTAAACCCCCTTCGAAGGGGG
TCTTCTCCTCTAAGGGAAAACCTTGTTTTGACATTTGCTTCAATGGGCC
CTTGATTTTGTTCCTTGCTAAACGGGTGCTAAACCAGGGGCCTCCTCTT

>Contig46

AAGGCTTTTGAATATTTGCACACTTTAGAAATGGAAATGTTTTTGGGGG
GCGAGTTGTCTTAATATTTTCTAGCTTGTGTGACATCCTTTTGA
AAGCAGCAATTCTGGCCTTTGTGAGAGATGGTGAATGCCTGCAGGTGTGT
GGACCAGTGCCTCCCTTCTTCTACATGCACGGCCCCCAGCTGGGCCCA
GCAGAGTGTGTACAGAATAATTTCCAAGGGCTGTGTCTTAACCTTTG
GTCTTGTCCCCCATTTGCTGTAGATTTGGCCAATTGACTTCATAAGTGCCT
CTTATGAACATAGATGTTGGCAATGGAAGTTGAGGACCAGTCAGTGGTTG
TTTTATTGAACACACAGCGTAAATCCCAACACAATGCTGACCTAAGAGAA
TTCCAGCCACTCTGATTCTCAGTCTCTTTATATCTGAAAGGGTTCTGTTT
CACTTTTCCCAGATCAAAATGTCCCTGCAGCTACTCAGCAGAGCTGTCTG
CAACTTATACGTAGAAGAGGTAAACAGTCCACAAACAGAAAGGCACAGGAC
GAGAGTGGTCTGGGTGATGCTTCTGTGGGGGAAAAGGTGATGAGGGTGC
ATCTGCACACCTATGTTTCATAGGTAAGTCTGGGAGGAGGTGACCTCCCCT
TTGGTTGAGGTGCTGAGGCGTCTTGTTAGAATGGCACTATTCCATTTATC
TGATGCAGTCTGTGGGAATTTTGTGGTATGGCCACCACAGGTACCATGCT
GGGAACAATGCCAGATACTGCCTGCTAAGCCACAGCATGAGTCACATGAG
CATTTGTGGGCTTTGGGAACTAAAGTTATTGAACGATAGTTATCTGAAAA
GGAATTTAGGGAAAGGGGACTTTAGTCCAGCGAACAGTTTGCAAACCAGG
GGGAAGGCAGCCTTCAGCGTAAATGAAGACGTGTGTGCCCCAAATAACA
AAGGGAGAGTTTGTCTTTTAGAGAGTAAATGTCCACGCAAGGTTCCTT
AGGCAAATGAAAGATGCAAACTTGCTTAGTTCTGATTTGTTTACATTTGC
TGAATTCGGATTGGTCCGTGCAGGCTTTTCTGGGAACTCCAAATACATGT
ATGACCTCTAGTCATACATGGCAAATGGCCGCTTGGCTCTAATTTGAATT
TAGGCCCAGTTAGTCACTCAGGATTAACCTTTTTCAGGGTTACAGCTCT
GAACAATGGACTTAGACCTGCAGGACATAATCTGTTCTTAACCTCTGGGAC
TACCTGTGCCTTTTGTGCTGTGCCAGTGAGCAGCTGTGGCTCTGGGCCCA
GACCCACAGGGCGATAAGGCACAGAGGTACGCATGGAGCAGGCTGTCTT
GCTGAGTGATCATGAAGATACACTTACATAGAGCAGCACTTTTCTTCCA
GTCTTTGTGATTTAACTCATTAGATCCTTATAACAAGAGTCAGTCCTCTA
TTTAACCCATGAAGCACAGGTGGAGTCCAAGCTTAGTTTGTGAAGGATGA
GCCAAAAGGATTCTTCTTGTAGACCTCAAGCTCAGCTCTCTCCATGGG
CCCTGGAGTAGGTGAGAAGGCCTCTGTCTTCCAGAGCCCACTGCCAATCA
TCTACATTTTCTGTAGCCCAATTCTAGGACATTGCTTTTACCAACTGAAG
GGTGAGAACTATCATAAGTTATAAAAAATCAATTGAAAAACAAAAAGGTAC
AGAACAGAAAATAAAAGATGAGAATCTATTAAACATAGTGATGTTACTGG
AAAAGGGGGTCTCAAACCAGACCCCAAGAGAGAGTCCTTGGATTTACAC
AGGAAAGAACTCAAGGTGAGTTGCAGGGTGGGTGAATTGAGAGAGTTTA
TTGAAAGCTATTCCATTACAAAGTAGAGCATCCTCAGACAGCAAGTGGAG
GAACATGCCATCATTAATTTTCTTATATAGGAATCTTGTCTATATAAA
GACTAAACTAAGCTGTGGCTATGTGTGGGTGGGCCGACAGCATGAAAACA
TTTATTCTCCTATTGATTTAAAGAGAACTATCCTTGACATTTTAGTGTGT

FIG. 4 (26 f 61)

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TTAAGTACATCAAAGCA1AACTATAATTA1CTTGAAAGCATATATTTT1A
TAGGGATTGGGACATCTGGGCTTTCTGTTGTTGTAGAAGTTTGTCTTGC
AGGGATTACCAAGCCACTTCCTTAGCTGTAAACATCTTAGGGCCATGGGT
CCTGACTGGCAAGGAATGTGTCTTGCTAGTTTAAAGATGGGCTTGATTG
AAAATGGTGTCCATCTGGCTCTCCTAGGCTCCTGCTTTCCTAACAGTAAG
GGTAAATGCTATGTTATGAAATGTCATTTCTGCCTTTAGCTTGCAAACCTC
TTGATGGTGAAATTTCTCCTGTCCGTTTTTCAGTGGGGTATTTATTCTGCAT
CCACGTCTTCACAAGGAGCTGAAAACAAATTGGATGGAAGCAACTGGGT
TTATGGGACACGTAAATGTTTTAATGTCATTTGGTGTGGAATTCAGATGT
CCAAGCAACATTTTACACTACAAATCTGCAACTTTAATAATCACTCAAAG
TACCTGAACCTCAATGCTTTCAGACAGACTTGGTATAAAGCCACCACCTC
TTTCTATTATGGCAGCCCTATCCTGAGGACACAAATTTCTGCAGGGCTTC
TGGCATATCTCTGATTAAACAAATGTCAACAAGGTTAAAACAAATGTCAT
CTCTGATTTGTTTGTTTTAAAGCCTGGATTTACTCATTGAATATTTCACT
CCTACTAGCATGTCTGTAGTAGTTTTCTTCAGGGACCCTAATTATTGCT
ATTAAAAATATGTGTGACGTACATGTTTTTTTTTTTATCAATTTGCAATG
AAAACCTTTAATTTGAATAATCTATTAGTGTTATTATTTGAAAGTGAAATCT
TTTCCTTTTGCTTTCTTGTTCTCACACATAGTCAGACAGTTTCCACACG
GGCTCATAAAAGGAATGATTCTGCCTTGTGTGAACTTTTTGCTTTATTG
TTAATTGCACCATTTTGTGACTGGCTTCTTGACCCTGTTGTAACCAAGCT
CATAATGTACATTATTTCTTATTTTGCAGTTGTAGACACTTGAGGAAGTT
CCCATTCTTTGTTTCTTCTTGCTTTTGTTCCCTGTGATAACTTTTTCATG
CAGACATTTTTTTTTTTTTTTTTTTTTTGGAGACCGAGTCTTGCTCTGTCATC
CAGGCTGGAGTGCAGTGGCATGATCTTGGCTCACTGCAACCTCTGCCTCC
CAGGTTCAAGAGATTCTCCTGCTTCAGCCTTCTAGTAGCTAGGATTGCA
GGCGTGCACTACCAACCCAGCTAAATTTTCAAATTAGCCACCCACCT
GGCTAATTTTTGTATTTTTAGTAGAGACAGGGTTTCAACCATGTTGGCCA
GGCTGGTCTCGACCAGGTGATCCACCCGCTTAGCCTCGCATAGTTGCAG
GTGCTATTCTGAGCTCAGGGCTCTGGCAGCTACAAGCCCAAGATGCGGTC
TCCAACATGTGGCCATTCAATGTGTCATGGCGCCCTCTACTGGTCTGGGAA
GCGCAGCTCTGCCAGTAGCTCCAGCAGGGCACAGCTGTTAAGTCGTGATG
TTCTACAGGTGACCAAAGGGCAATCTCTGGACTCCTTAGCCGCTAGGTCC
TCTCTGTAGCAGGACCCAGGAGAAGGCAGGGGCTGAGGATGGCTCTCTTA
GACATTTGTGATGAACCAAACGTGTGTCATTCATGAACTTCTGTGAGCAA
GCAGGTGAGTAGAGTTGGGTTATAAAAAGTCTTAGGGTCTCACTACAGAG
ATGGACTTGTGTGTAGATGGTGCAGAGCCGCTGAAGAGTTCTACTTGGG
GTAATGGTGTGATTGGGTTTTCGTTTTAGGAAGATTTCTTGCCAGAATG
AGGCGGGCAACCCAGAGCAGGGAGTGGCCACATGTGGGTGTGCAGTTATG
GGCCACTAATCCAGGTGATAAATGGTGTCTCTGAACTTCAGGTGGGGGTG
CCACATGTCTCCATCTGCTCTGTACCCTTGAGACTGGCCTTATGGGCTGC
CTTAGTGGTCTGTTGTCTCTATCTCCTGGTTGGGCTCAGGCAATGGGAG
ATCAGAGGGAGGAAAGAGAGCTTGGTTAGAGTGCACCCGCGCCCTTCAG
GTTGGCAGTGGCCACATTCCCCTATACAGAAGGCCACAGTTTCTGTGAGT
GGCCCTCCCAAGCCCCAGCTTTCTCAGTGGGCCAGCCACCTCCCCATCC
CTTGCTCCTCCTCCTCCAGAGAGGGTTGTGGATTTCCACTGTGAGCAGTG
CCTGGAGCTCCACCATCTCCTGCTGCTTCTCCTGACCTGCCTGCAGTTT
TATAAATAACCTTTCTTACATTACCTCTAGCATGCACCTTTTGTGTGTA
TACTCTGCCCCCTGTGAGCAGCATGACTCATGCCAAAGAGTTTGAATTTTT
TTCTCCAGGCAACGGGAGGTCAATTGGAGGATTTTAGACATTGAGAACAGA
TGTGTATTGTGGAAATATCTGTCTGACTGAAGTGACCAGGATGGTCCAAA
AGAGCGAGAATTTGAGGCAAGCAAACCATCAGCAGGCCAGCAGCAGAAAT
CCAGGTCTATAACAGGGAAGCTGAGGCTCACAGGGTTGGATCAGGGAATG
GGAGAGGGAAGCCAAACAATTCCATGAGCATGTGAGTTGCACATATGACT
TGGTAACATATTTTATTTTTATTTTTATGTTTTGAGACAGAGTCTCGCTC
TGTACACAGGCCAGAGTGTAGTGGCATGATCACAGCTCTCTGCAACCTC
TGCCTCCTAGGTTCAAACAATTCTCCTGCCTCAACCTTCCAGGTAGCTGG
GACTACAGGTGCGCACCCTACACCCAACTAAGTTGTGTATTTTAGTAG
AGATGAGCATTACGCTGTTGCCTTAGACACGG
>Contig47
AATATTGATTATTTGACCAGAAATTCATGCAGCTAACCGTGACCCCTGGC

FIG. 4 (27 of 61)

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AAAATAAAATAGTGTAT...GTACGTGCAATATACATGCAAAGAAATGAG...
GAAACTAGAAGGATGTCAATCAAATGATAACATGGTCATCTTGGGGTCGG
AGTACATTTGGGGATGAGGGGAGCTGTAAAAGCAGACTTGGACCTTTTCT
TCTACCAGTACCGTGTCAATTTGAATTTTGGAAAGAAAAAAACTCAG
AAGGAGGAGAACGAGCAGGAGGAGAAGAAGATGGATCTTAAGTGATTTGC
CCGGGAGCACCTTGAGAAGGTGAGATTCAAGTCTAGGTCTAAGCTTTCTA
ATTCCATGAGTGGGAGTGACCCACGTCCAAGAGGAAGCTCAAAAGGAAGA
TGTTCTCCATCATCTCTTGCTCATCCTAACAGCATGCAAACACATCCA
ATGCAGCTCAGAAAACCTCCCAAATTGCCAAATTTATTGGAAACACTTAA
TGCTGTGGTTTCCAATTTCAACTGTAAAGTAGGTATGTATGCCATTGTTA
CCATTAACCTTCTCAGAAATGGAGAGAGCTCTCTTCCGCCTCCTCCCCCT
CTGCTGTGGCTTTGGTGAGACGTGCACTCAGGCTCACCTGTCTCCATGAT
CTCCAGTAAGTACACATGAGCAGAGAGGCTCAGCTCAGCTCTTCTGGT
CCCACCAGGGTTGATTCTTTGAGAATTCTAGAATGCCACATCCTAGGCCC
CCCAAAGAAATCCTGCATCTTACCCCCAGAAATATGAATCATAGCAAATT
TCAAATCAACCTCGTTTAATACTCACAGACTGGGCACATCCAAAACAT
ATTTTCAGTTTTTACAACAGTGCCTGGTGATATCGGCACTATTTGTGGAA
GCAATAAATCGACACGGAGCTGAAACACAAACAAATGCCAAATTGTTTTT
ATAACACCTGATTTTTCTTTCTGTTTCTTTATGCAGTTTAGTTTTGTTTTG
CTTAACCTACCTCAGACCATAGTCTGGTAAACTCACCACCCAGAAGCTC
CCTTGAAATGTGGGTATGCAGCCACTAGGTGGCAGGAGAGAGTTTCTCTGC
CTGGAGGGAGGACAGCCACTCTGTCCCCGGGTGAGGCCAGGGCCACCCTG
CTACCTGCAAAATTAGCATGGGGCTTTATGAACCACAGCTTCCTAATAAA
CACAGGATCTGTTTGATAGAGACTCCAAAACACGCCTACCTAGTGATGAA
AGACTCAACTTCAGAAGAAAACCTTCATGGCAAACATCTTCAGAGATGTT
TCCAACCTTAAGGTTCTGAACACAGACGCTTCCCAGAAAGCCATTGTTTC
TCAGCACCTGGGAGCCTTGCTTTGCTTTGCTTACAGACTCGCTGTTCTTA
AATCACTGCCAAGATAACATCTGTCTTCTCTTACCTCTATTTTCGATA
TAAGGACTCCTCACTCTTGTTGCTTCTTATTGGCTACCTCTCCACAGGGA
GAAATCGCTGATTTAACAGCAGTCAATATCCCAAATCTGGAACAGGGAAC
AGGGAAGCATTTAAAAATTGGAGAATTTAGGCCGGGCACAGTGGCTCATG
CCTGTAATCTCAGCACTTTGGGAGGTGACGTGGATGGATCACTTAGGAG
TTCGAGACCAAGCCTGGGCAACATGGCGAAACCTCATCTCTACAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAACCCAAAATTAGCCGGGCATGGTA
GTGCACACCTGTGAGCCCCAGCTACTCAGGAGGCTGAGGTGGCAAGACTG
CTTGAGCCCTGAGGTGAGGCTGCAGTGAGCCGAGATCACACCACTGCAC
TTCAGCCTGGGCAACAGAGTGAGACCTTGTCCCAGATAAATAAATTAAAT
TAATTTAATTAGGATTTTAAGGATTTTCCCTACAGACACCTCCTTATTT
TCTCTGGCCTTTTCTGACTACTCTCCCTAACTCCCTGCTCCTCTGGTCTC
CCAAAACCTACTCCAGAAAAAAAAGGGGGGAGGGACTAAAGGAAAGCC
AGGTGACAGTGCCAGTGTGACAGATGACAAAGCATCTGCCCGAACAAACC
GTAGGTCCCTGAACTTTCTCCAAGACCTGTCTGTGGACTTACCTATGAAA
ACCACTTTTAGCAAAAACCTCCTAAGCCAGTTTATCAAGATCCCTTAT
CCTCAATATCCATCTGATTGGATTCTTCATCCCCCACCATTCCCCAGTGA
TGTCACCAGGCCTTTCTTCAGCAACAGTAGTTAGTGGGTGTAGCCAGGAC
GCCCCCTCACCCCTGATATGCCCTTTTAGTAATTCTTCATCCACAGGTTT
CCACCTGCTCCTAGGCTATACATTCCCATTTGCCCATGCTGCATTGGA
ATTGAGCCAGTCTATACTGAGGTCTTACTTCACCTCTCGCCATAGTCC
TGAATAAAATTGGTTTTTACATTTAAAAACTGTCCAGCTCTGGTTGTTCC
TTGACACAGGGTAATTTTTATTCCATGTGATAGTTTGCCTTACCTCAGCC
TACACCCCTCAAACTGCAACTCTATATTCAAGAACCAGACAGCCCTTTC
CAACAGATAGGAAGAGGCTGCCCTGGTGCAAAGGAAGAGGCTCTGGGAGG
AAGGAGAGAACCCGAAGGCTGCCCCCTCCTCTAGACTGAGCTCTGGGATG
GGTGGACGATAAAACCCAGATACGTTTAGACATCTGAGCGTGGAGAGGAC
TTTGCTTTGCTTCCACAGGGACCCCAAGGAACTGCAAGCCCTCCAGAGA
CTAAAAACAGCAGAACAGCAAGAAATGGCAGCAAAGGTCTGGGCAGAATC
ATCCTATGTGGGCACAGACACAAACAGAGTCCCCTGTGGCCCCAGGAGAG
TTTAAAGAAGATCCAGAGGCTGTCTATTCCATATCTCAGCAGAGACAGG
CCCGTGAGCCTAAAAGCTGATCATTAGGACAAGAAGGACACGAAGTGTCC
TGCAGCGTGAACCGCGTGGAACAAGGCCAATCACCAGACACCAGACCAGC

FIG. 4 (28 of 61)

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CAGACACAGCCCCGAGTTCCTCAAGACCACCACGGACCCATCGCCCCCTC
ACCAATAGCTCCAGGCTACATAGACCCCTCCACTTCATGGATGTCCTCA
GAGCAGAAAGGGGAGGCAGGAGTGGAACCCTGACTTGGTTTCAAGTTGAAAC
ATAAAATGACTGTACTATTATTGAATTGCTGAAGTTTACGTGAAAGAAAT
GAGATTTAGTTTTTGGCCACAGTGCAAAATAAGAAACGAGGCTTCAACTG
AGATTAAGGTGAGTTATAGGAAAATGTACTCCCTTGAAGGACCTGTGAAG
TGTTGTTTCGCTATGAGAAAATGACCAGAATCCACGTTCTTAGCTGCGGGAC
TCAGGCTGACTCCTGTTTCTGGAGCTTGCAAAAGGGCAGGGAAATCCCT
GTTTCAGGCACAGTGATTTCAATGTTTAAAAGAAAACAGGTGGGCCCTGG
CAATCATGATAACATGTCATAAGTTTACATCTCTGTGAGGCAGGTAGTGT
AATCCCCATTTTGCAGGAGGAAACCGAGGCTGAAAGCAGCTACATGGT
CTCTTCAATGTGGCCCAAATGTTGGAGAACAGAGCTTAAGTGAATCAGCA
ATTCTATACTTAGAACTGACTCTCTCTTTATTATATCTCACTACTACCTT
GATATTTGAAATATTCAACTTTTTTCAATCAAAAAATAACAATAATTTAG
GCATAATGACTACTATGTCATTTAATTTCTTGCTGATATTTCAATATCCC
ATGCCAGGAATATTGAAAGCTCAGCTCCTTAAGAGCTGACTATGGCATCA
ACTCCAACAACCATCCTTCCAGAAATATTTTCCCTTTCTTTTGTATATA
GAGTGGCACTGGCCCTATATGGTGACCACTTGCCACATGTGGCTGTTGAAC
ACTTGAAATTGGCTTGTGAGAATTGCAGTGTAAGTGTAAACACATACC
AAATTTCAAAGACATGGCACATAATAAAAAATGTAAATATCTCATTAAC
AATTTTTATATTGACTGTGTAAGTAACATTTTGAATATATTGGATTAAAT
ACATGGATGATGCCCCAACACCCACAGTCCCTTATCAAGTCTCTACTTCA
CATTTTTGTACTTCTGACTTAGAAATAGCACTGGCGTCTAAGAGCCTATT
AATGTCGTCAATAGGTTCTTGGGAACCAATTTTAAACAAAATGACATA
TAAGAAAACGAATAACATTGAACAAAATGACATTATTCGAGGACCTGCTG
CATGTTGTTTCACTTAAAGTCAGTGTCCAAGAACCTATCAGTGACATTTA
GTGAGGACTTGCTGTCTTCTGTTTACAGGAACCTGGGCAAGTTACTTA
ATTCCTCTAAGCCTGGTTTATATCCCTGCAAAGAGAGAAGGATAATAATC
ACCGTACTTAGTGATGTCGTAAGGAGAGAAAATAAAATAATAATATGAAA
TGGCTGACAGTGCTTGTGTCACACAGAAGATGTGTGATCCACAGTAGCTG
CTATTGTCTGCCTCACTTCACTAGTAATGGTCCAGGGAGGCCTTTAATGT
GCATGGTGCAGTACATTACATGTTGGACATGGGTGAAGGGAAAGACCAG
GCTCATCTAAACACAATAGGATGCTTGTGGTGTGTTTGGAGAGGAATCAAG
GACTAGTTATCCACAGCTGTAAATGTCATGGATCAAAGAGATAAGGCAC
ACAAAAGACTTTGTGAGTAGCAAAGCATTACAAAATGCAGAGACCAGCTG
TGGGTGGTGGTGAGTCAGACCCAGCTTCCCTCTGTGCCTGGCTGAGTGGT
TCTGGGCAAGTCACGCCATCTGTCTTGATGCCCTTCCCCATCTATAGAGA
GGGAGCAACTGAGGCCCTTCCAATACTGAAGTCCTTTATTTCTGCTACT
TTAGAAATATCCACATTTTGGTAAATTCAAATGATCCAATGATTCCATT
TCCTAATGTTTCAAAACTAGCCCCAGAAACATCTAAATGAATCAAACAAAT
AAAATATTTATTGTGTATGTTTGGATTGCTGAAACTTCTATTTTAGCAAC
ACACACACACACACAGAACCCATAAGCCTTCATCTTTCTTGGATAAA
CGAGCCTTCTGTCTGGCCATTTAAGTCACGATTAAGTAAATGATTTCCA
ACTCGCCTTTTGCAGCAGTTTCAATGGGTCTTCTGCGTGGCAGTGGCC
CTCCTGACTTATGATTTCTGTGTGTGCGCCTGTTACCACTGCAGCTTAA
CTGAGGAAACAAGAACAAAACAGCTTCTGACCCCAAGAGACTGTTGGAGG
CAAAGGCTTCAGTCCCAAGAACCTCACACGTGGGGAGCCCGAGAGCCCAG
CCCTGACCTTTTCTCCAGTAATAACATAAGAAACAACAGGCACTGGCCTT
ATTTTGGATACAAAGAGTGGTGCTTTTCTTAAATCTTCTTTAGTCAGG
GCTACCCCTTCATGGACGCCCCAACATCCATGGTTTCTGCTGAGTCCCT
GCTTCCATATTCCTGCATTTCTCACTTGAATATCCCTGGAGTACGTTAA
GCAGCCAGGTTTGGAAAGTTCTTGCTGTGCAGGCGGGTGTGTGCATGTCCT
CTCTCTCAACAGGACACAAGCTCCCCAAATCAGACGGTATGCCTCCACGC
CCCTTCCCAAGCCTCCCCAGCAGCACCGAGCATGTGAGGGGAGCTGGGGC
CCAGGCCATGATGGGAAGCACTCTCTGCCTAAAGACTAGGGTGTGCGCC
CTCAACTGTGGGAATGAGCCCCAGCTCTGGTGTCTGCCTCGGTTTTTCTT
CCTGGACAATCAACATGAACTCCTCACCCCTCTTATCCACTTTGCATAAA
CTGAAAATAACAAACCCAGGGCTCTTCTGTGCAGGAAAGGGTTTTTTT
TTATAAAATTAACAGAGATGATTCAACACACCCAGGATATAACACATGG
GCCATGAATCAAGGCAGCATTGCTCTGGTCAGCCTGTTGTTTGGGCCCC

FIG. 4 (29 of 61)

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CTTGGCAGGGCTCTCCCCGAATCTTCCCCTCTTGACTCCCATCANCACA
GCACTCCANCTTTGTGTTACAGGCGATAAATGGGAAAGGGGTAAAT
>Contig48
CATTCTTAATTAGAGAAACGCTCATTAACTAGACACCCAAATTCTCTGG
GGGGGATCATTCTTACAAGCATGCCCTTCTCTCTTAAAGAGAGAGCACT
TTTTTCGCAAATAATGCTGCCATGAACATACGGGGTGCATGTATCTTCGT
AATAGAATGATTTCTATTTTGGGGGTATGTACCCAGCAATAGGATTGCT
GGGTCAAATGGTATTTCTGGTTCTAGATCTTCGAGATCTTCCACACCGTC
TTCCACAATGGTTGAACTAATTCACATTCTTACCAACAGTGTGAAAGCAT
TCCTATTTCTCTGCAACCTCGCCAGCACCTGTTATTTCTTGACTTTTTAA
TAATCGTCATTCTGACTAGCATGAGAGACAGTATCTCGTTGAGGATTTGA
TGTGCATTTTGCTAATGATCAGTGATGTTGAGCTTTTTTTCATATGTTTT
TTGGCTGCAAGAATGTCTTCTTTTGAGAAGTGTCTGTTTCATGTCCTTTGC
CCACTTTTTAATGGGGGTGTTTTTTCTTGTAATTTGTTTAAGCTCCT
TATAGACTCACAATAACAAAGACATGGGATCAACCTAAATGTCCATCAAT
GATATAACGGATAAAGAAAATGTGGTACATATATACCATGGAATAGTATG
CAGCCATAAAAAGAATGGGATCATATCCTTTGAAAGGACATGGATGAGC
TGGAAACCATGATCCTCAGCAAACATGCAAGAACAGAAAACAATTGTTG
CATGCTCTCACTTATAAGTGGGAGCTGAACACTGAGAACAACAGGGACACA
GAGAGGGGAACAACACACATTTGGGGCTGTCAGGGGTGAGGTGGGGGAG
GGAGAGCATTAGGAAAAATAGCTAATGCATGCTGGGCTTAATACCTAGGT
GATGGGTTGACAGGTGCAGCAAATCACTGTGGCACACATTTACCTATGTA
ACAAACCTGCACATCCTGCACACGTACCCAGGACTTCAAATAAAGAGA
GACAATACTTCTCCCTTAAGTGTCTACTGTTGCTTTGCAATAAAAACTTC
CTGCCTTTCACCTTCACTCTGACTTGTCCCTGAATTCTTCTCGTGATGGT
GTCAAGAACGTGGACACTGGCTGGGGCTGGAGACTCACCAGCATCCGGAG
ACCCTCCTGAGCCCTCCAGCAATACAACTTTGACACAACTATGAAATCA
CAGATCCAAGAAGCTCAAAGAACCCAAGCACAGGAAACATGATGAAACTA
CATGAAGGAACATCAGAATTGAATTGTTCAAATCAGTGATAAAGAGTAA
ATCTTAAAGCAACCAAGAACAAATATCCATCATATACGCAGAAATAAAG
ATAAGTATGACAGCAGATTTACAAATAGAAAAAAAACAGTGCAGCAAC
AGAAACAACTATCAATCCATAATTCTATACCTAGTGAAAATTTCTTTCA
AAACAAAGGTGAAATAAAAAAATTATTTTCAGGAATACAAAAGCGAAAAA
ATTAATCACTAGCATTCTCACTGCAAGAAATGTTAAAGGAAGTCCTTTA
GGCAGAAAGAAAATGATACAAGGTGAATATTTGGATCCCTGCAAGGAACT
AAAAAGATCCAGAACTGATACTTAATGGGTAAACATGTAATTTTCATCA
ACAAGTGAATGAATAAACAAATCATGATATATCCATATGATAGACTACTA
CTTAGAATACAAAAGAAGAACTACTTATGCATGTGATAACATGAATGATA
TTCAAATTTATTATTGAGTGAAAGACACCAGATCAAAACAAAGTACATAC
TGTATGATTCTGTTTATATAAACTCTATAAATTGCATGCTCTTCTATAG
TGACAGAAAGAAGATCAGTGGCTGCCTGCAGACAGGAAGAGATTACAAAC
GGAAATGAGAATTCCTTAAGAGATGATGGACATGCTCATTACCCATCATA
TGTATACAGCCATAATGGTTTTACAGATACATATATATGTACAGCCAAC
ATAAATATAAGTTATCAAATTACAGTAAGTTCTGACTTAATGTCACTAGG
TTCTTGAAACTTTGACTTTAAGCAAAATGATGTACAGTGAAACCAATTT
TACCATAGGCTAATTGATATAAAGATGAGTTAGGTTTTTGGTTTTTTTTT
TTTTTGACATGAAGTCTCGCTCTATCGCCCAGGCAGGAGAAGAAGAGTTAG
GTTTTACAGCATGTTTCTGGTCAAGAACATCATCAAACCTTGTAATAA
AGGCACAAAACACTTCTAATATTAAATATCAAAATAAATATGAGTTATAC
AGAATTTAAGAAAGATTAATAAAAAACAAGTAAATCATTATTTATGGGAT
TTTTGGTAATCAGTGAGTTATGTGGTCAATAGTGAAGTGGGGTTAAGTCAA
GAAATAAATGTTTGCAAAACAAAAATTTTAAAGATCCTCTCCTACCACCA
CACAAAAACAAGAAAACACGGTGGGCTCGCTAAGCACTTTTGTACCACT
CGTATCTTATGCGTTTGTATGATTATTGTAAATGCTTTATGATAATTTTT
AGAGACAGGGTCTCACTCTGTGTCTCAGGCTGGAGTGAAGTGGTGCAATC
ATAGCTCACTGCAGTCTCAACCTCCCGGATTCAAGAGATCCTCCACCTC
AGCCTCCAGTGTAGCTAGGACTACAGTTGTGTGCCACCATGCCATCTAT
CTTCTTTTTTATTTTTTGTAGAGACAGGGGTGTGCTTTGTTGCCAGGC
TAGTCTTCAACTCCTGGGCTCAAGCAATCCTCCTGCCTCAGCCTCCCAA
ATGCTGGGATTTTCGGACATGAGCCAGCAGCACCTTGCCAGCATTATT

FIG. 4 (30 of 61)

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TCATAATAATTATAAGTCATTCTTCATTTCATCTTACAACCCACTTGTTTC
CAGTTTCAGGATCTCGGGTGACCAGAACCTATTAACGTTACGCACAAGTC
AGAAACCAGCCCTGGACAGGACACCATCTACCGCAGGGAGAACTTACAC
ACCCACACTCACTCAGACTGGGACCATGCAAAGAACCTAACGTGCACTTT
GGAATGTGTGTTCCATACCCACTAGAACAGCTAAAATTTAAAAGACTGAC
CATACTTGAGTGTGTAACAGGATGTGACACAATAATCTTTTAAGCGCT
TCFGGCTAAATGGCACAGCCGCTTTGGAAAACAGTTGGCAGTTTTTCAAG
TTAAATATACCCAACTCTATGATCCACTTCTCAACAATCAAACAAGAGA
AATAAAAGCAATGTCTACACAAGATGTATACACAATGTTTCATTGCAGC
CTTAATTATACAGCCCCAAGTTGAAACAAGCCAAATGTCCATTACCAGA
TGACTGGAACATACAAATTTGTGGTATATTGATACAATGAAATACTACTTA
GTAATAAAAAAGAAAGAGCTATTAACATAAGCAACAACATGGATGAATCT
GAAAACAATTATGCTAAGTGAAAACAGCCACACAAAAGTTACATACTGTA
TGATCACATCTACATAAAATTACAGAAAAGGCAAATAATCTATAGACAG
AAAAGCAGATGAGTGGTTACCTAGGGATGGGGCAGAAGGGACGAAAGGAT
GGATTGCAAAATAGCACAAAATATTGGAGGGATGACAAATATATTTCATT
ATCTTGATTGTGGGGATAGTTTAATGGGTATATATAGAGATCAAAGCTCA
TCTAATTATACACTTTAAATATATGTATTTTCATTGTGCATCAGTTATTCA
TCAACAAGACTATAAAATAATATATGCCTACATACATTTTTAAATATTCA
AAATCTCACAGTTATATACATAAATGCAACTGAATATGTATTTCAGATGTT
TTAACAAGCAGAAAGGACTGATTAACTCATGACAGCGCTGTTTCTGGG
AAGGGTGTAGGAGACAAGAGATGGAAGAGGATGAGAGCCAGAAGAGAC
CCTTGTAATGTTTCTTTCTTTTAGTAAAAATATATTGACAGTTAAAGCT
GAGAGGTGAGAATAATAGTCTCATGGCTTTTGTGTCCTTAAATTTTACA
AACTAAGTGAAATGGGAGAAAGCAAAAAATAAACTTAAATAAATGTTAT
ATTGCCCAAAAGAGATTTAAATGGAGGTTAGACACATGAGACTTACGT
TCTCAAAAAGTAGAATCTGCAGGGAAGTTTAAACAATAAAGAATTAA
AATCTAGCTTCTACCAGCCCAAGCCTAAAATGTTCTGCTTTATTCTTCC
TTATTATAATTATAGGTAATATATTTATGTTTGCAAATGAATGCAGTG
ATATTAGATCTCTAAGAGGTGCTAAAAATGAAAGTACATATTCCAATTT
TTCCCAATTTTCTTCTCTTTCCATGAATGAAAAATATACATATTTGATG
ATTTCCAAGTTTATACAACCGATCTTCTCTTAGTTTCTCTTACCAAAT
TCCCTCCCTCACTCAGAGAGGGAGATCTGTTATAAATGCTGCCAGGAGGT
AGCCCTCATACCATCCACACTCTCATCAGGATCCTGCCTGACCTGCGAGG
AGCAGCAGCAAGAAGGAGACAGAACCTCCACGCTGAGCATCTCAGGGCTT
TCTCAGAGACTCCAGAGGACCCTGATAGGGACAGAGCCTGGCCAGCAATC
CATGCTGCCAGCTGTATGATTGTGGGCATGTAAATCTCAACTGAAAATG
GGTGTATAATAACATGTTCTTCCCAGAATGAGCTTTATGAAGATCATAT
AGCTGTTTGGAACTCAGACAAGCACTGGTAGGAATACAAACAGGGGAGCC
AACAGCCTATAAATAACTTTAAGAAAGGGCATGAATGTAATTACTTAG
GAACAAAAGGCAAAGTGAGAGATGCCTAGGACTGAGCTGGACAAGCTGC
ACCCCTTAGTGGCTCAGCCCATGGGCTGACAAGGAAAATGGAGGAGCTAC
CAAAGAAGGTGAGAGGATTCTGGGAGAGTGGCCCTCACCCTGCCAGGGC
AGGGCTCAGTGGGAGAGAGGGAGATCTGTTATAAATGCTGCCAGGAGGT
GAGTCATGTGAGAAATGTCCATGTGAAAACATCCACTGTGTGTATCTAAAG
AGAGTGGCTGTAAAACAGGTGAGGTCAGGGTCAAAGGTCTTATTGTCTCAGATGT
TATCTGCATGCATTGTCTCACGACCAAGAAAATAAGGAGCATGGACACA
AAGGGTTAGGTTGAAGCAAAAATTTAATAAGTGAAAGAAGAAGGCTCTCT
GCAGTGGAGAGGGGAGTCTGAGTGGGTTGCCACTTTGACAGCTGAATCCA
AAAGCTTTTATAAGAACTCTTCTCATATCTGCAGCTGTTTGAGTAACCTT
CTCTTACCTATAAACTGTCTGTATACTCTCCCTTATCTATGCAGCTGT
GGGATGTCTCCAGGTAAGCATAAAGTGTAGCTTCTCTTGTGTTGTATACT
GTGGGTTTGTGTTTAGGCAAGCCCCATCCCTCCCTGTGTAAGCTCCCAT
GGAGCCCACCATGTGCATATCTGAGAAGTGGAGGAAGCTTTCTCTGGGAG
CTCACTGATCGTACAAAGAACAAGAGGCTTCTGTGCCGCTTATCTATTCA
GGTGCAGCCTGAGTTTTTCCCAGGCTGCTCTATTTTTGCCTGTAGCTATG
ATTTTTCAGGCAGGCTGCTTCTCTGAAGACTAGCCTTAACTGTCTACCTA
TCAGATTTTTCTTTTCTTCTCCCTCAGCTGGTTCCCTCACCAAGGCTG
AGCAAGTGAAGAGGAGGGCACAGGGCAGGCCAGTAGTGAGCAGCAACAAG
GAACTAAGACAGCAGAAACCACTCTTCACACCTGGGTTGAAAGGGGTGGG

FIG. 4 (31 of 61)

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GAGCCAGGACTACAGC1 CAGGTAAGAACATAGGTAAAGAGATACTGTTGT
TGTGTTGTTTTTA ACTATGAGAAGCATTGAGCTTTAAATTTCTACAGGAA
GGATCCAGTTT CAGACAGGAGCACCCAATATTCAGAAGAGAAGAACATGGT
GTAAAGGTCCTGGGAAGGCTGAGAGGATTGGGACTCAGAATCCAGAGCAG
AAGCCGTCTGTGAACAGAAGAAGGACCTCCCCCAGTGTAGCAAGAGGGAG
GGAGGAGGGACAGATGCCAAGATGGTTT CAGGAAGAAGGTTTGGTGGTAAA
TGTGAGGCTGTGCTCACCTGCTGGCTTCAATTTTCTCTTTAAATGTGAG
ATGGAATCATTTGATGAAGGCCATGCCATGCAATGAAATGGCAGTCTGAG
GCATGGAGCAGCTCCAGCTTAGCCCGTGTTTAGGGTAATTATGGCTCCAA
CCCAGGAGATGAATATGACTAGGGAAAGTGAAGTCCAAAAACAAATGGTC
TCAAGTTGACTGTGAGTCTTCTGGGAGGCTGAGACGACAGGTGGGGTTGA
CAAGGGAAGGGGAACCCACCTGCTGAAAAACATCAGGCTGTTGGCTGGGG
GAGGGGTGAGGCCCTGTGTTGTAGAGATGGATGGATGCCTAAAGTTGGGTA
AAGGTTTTCAACTCTACCCTCTGCTGGGTGTGGAAATAAACAAAGACCACC
CAAATGAGAACAAACAAAGACTATTTATCCAGAGCTTGCTCTGACAAGGG
AGTCGGCAACCATCACTTGCTTGGCAGAGACTCAGAAGTAAGCAGGGGAG
AAAGCCTCATAGCAGAAAGAAGGGAAGTCTTCATGTATGCCCTGAGTGGC
AGCTGTAGATGTGGGTGAGTTGCAGGTGGCTAACTAGAAATGGGGGACTC
CTGTGTGATTGATTAGGAGCATGTTTGGCTTTCTCTGGTTGGTCCTACAT
TGGAAGAGGGGAACAAAAATTTAGGGCAGTTGTGAGTTATTAATCAAGTG
TTGGCCATTTTTGACTGACTGTTTACAGGAGTGACTGGCTCCCTGGATTGT
TTGCTAGAAATAGTGGTCTTCACTTCTGCAAGTCTGACTTTCTGGTAAT
AGGCTTCTGGGTGGCTATTGTGGATAATAAGTGGGTTTTCTGAGCTGA
TTTCTGCAGATTGTGGATCAGAGTTATTTTATATAAACAGTCTGACCATT
TTCCACTGGCATATTCCATCTTCCAAGAGCTGGCCAAGCTGCTGTCTTAT
CTGTCTCCCCCAGCCCCCTCCACTCTGGCTGTGAAAATACAAGCCACTAGG
TGAGGAATGGGGACAATTGAAGACTGAAAGCTTTTCTTTGCTGGGTTCGC
AGAGCTGAGGAAAGAAATGACAACATCCAAGTGTCTGCCCTGGGCCAGTT
TTAGGACTGTAGTGGTAATGCAAGGACTGTGTGAGTTTATATTTTCATTT
GTCTCTCTAAGGTGGAACAAAAACAGAAAATTGTCTGTCTGCA
GTCTCTGCAAAAGTCTAACACTGTGCTTCCCAACATTGCAGCCATTAGCC
ACAGGTGAGTATCAAGCACTTTAAATGAGACTGGTCCAAACTGAGATGTG
CTCTGAGAATAAAACACACAGCAGATTTCAAAGACCTAGTACATGCCCTG
ATTTCAAGCTATATTACAAAGCTGTGGTAATCAAAACAGTATGGCATTGG
GAAAAAATAGACACATTGGTCAATGTGACAGAATAGAGAGCCCAGAAAT
AAACCCGTGCATGTATAGTCAACTAATCTTTGACAAGAGTACCAAGAATA
CACAATGGGGAAAAGTCTCTTCAATAAGTGGTGTGGGAAAAC TAGATATC
CACATGCAAAAGAAAGAAATTAGACCCTTGTATTACACAAAATCTAAAAT
TAATTCAAAATAGAAAAGACTTACATGTAAGATCTAAAACCATAAAACCT
CCTAGAAGAAAACATAGGGAAAGAGCTCCTTGACACTGGCATTAGCAGTA
ATTTTTGATATTAACATCAAAAGTACAGGCAATGAAAGCAAAAACAAGT
GAGAGTATATCAAACTAAAAAGTTTCTGCACAGCATAAACAAATCAACAGA
GTAAAGACATGACGTATGGAATGAGAGAAAATATTGACATCTGACAAAGG
GTTAATATCCAAAATATATAAGTAATTCACACAACTCAGTAACAAAAGCC
AAATAACCTGACTTTTTTTTTAAATGGGCAAAGTACCTGAATAGGTATTC
CTCAAAAGAAGACATACAAATGGCCAAGAGATGTATGAAAAGCTGCTTAA
CATACTAATCATCAGAGAAATACACAAATCAAAACAAGATATCATCTCA
CACCTGTTAGAATGGCTATTATTTAAAAATGAGATAAGTGTGGCCAGGT
GTGGAGGAAAGGAAACCCTTGTACATTATTTCATAGGAATGTAAATTAGTA
CAGCCATTATGGAGAACAGTATGGAGATTCCCTAACAAAATTTAAAAATAG
AATTACCATATGACCCAGCAATTCCACTTCAAGGAATACATTCAAATACT
ATCAGTATCTCAATAAGATACTTGCACTCCTATGTTTCGTTGCAGCGTTAT
TCACCATAGCCAAGATACAGAAACAAGTTAAATGTCCATCAACAGATAAA
TGGATAAAGAAAATCAGGTACATATATATATACAAATGGAATATTATTAG
CAAAATCCTGACATCTGAGATAACCTGGATAAACCTGGAGGACATTATGC
TAAGTAAATCAAAGCCTGACACAGAAAGACAAATACCACATAATCTCAC
TTACATATGAAATATGAAAATGTTAATTTTATGGAAACAGAGTAGAATGG
TAGTTGCCAGAGCCTGAGAGTAGAGAAAATGAGATGCTTGTCAAATCAAA
TCATCACATTGAATATATATAATCTATTTGTCAATTAAATATTTTAAGAA
TAAAAATACCTGGCACCACAAAAAAGAAATGCAAAATGTCTCAACAATGTT

FIG. 4 (32 of 61)

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ATATGTATTGCATTTTG, AGTGATAATAATTTGAATATTAGGTTAAATAA
AATATATTTGAAAAATTAACCTTCACCTATTTCTTCCATTTTTGTTAACA
TAGGTACAAAAAAATTAATAATTACCTATGTGGCTCATGTAGGTGGCTC
ACATTATACTTTGATGACACTATACAGGCTGGTGACCATATATCTCTTAG
ACTAGTCTAAGTGATTAAACAGTGGTTCCAGAAAGATCCAGGTTTAACAC
CAATGAAAGGGCCAGCTGGCTTAGCCCAGCTTGTGTGGGAAATGTTGGGG
AGTGGTTTTAAGACAGGGAAAAGCAAACTTTTGATGCTATTGACTTTTTG
AAAAATCTTTTGTGGCTGAAAAAACCAAAACATTATT

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GCTCGAGTGTGTCTCTAAAGCCTTTCCCCCATTTGGCTCCACTATACGCAC
TCTCCTGGTTTCTCCTCCCTCTAGCCGCTGTCTTGGTCTCCTTTCTGATT
TTGCTGCGTCTCTGTCCCCTGAATGATTGCTTCTCCACTACGGGGTGAT
TTTGCTCCCCAGGGGACATTTGGCAATATCTGGAGAGGTCTATGTTGTG
TTTGAGGGTGTTGCTACTGCCATCTAGTGGGAGAGGCTAAAGATGCTGT
TAATGCCCAGGACAGTCCCCATAACACAGAAATTATTCAGCTCAAAATATC
CATGGTGCCAAGATCAAGAAACCCTGCTCAAAATATTAGCATGTGCTGAAG
GCCCTTCTCTTTCTTTAGCAATATCTGCCTCCTTAGGGATCTTTCTAG
TCTCAGTGGTTTAAACATTTAAAATCCCAAATTAGGCAATAAATTGGGCCC
CAAACCTCGTTAGTATAAAATGTAGAAGTGTGTTATTAGAAGGCTAATAA
AATGACCTGGTGAGCATCTGCAGCTAGCCTCTGAGCAATTCTGGGGACCA
CGTGCAAGATAAATCCATCTGTTCCCTCTCTGTAATGTGGCGCTACCTTG
TGGCCGATTTTTCTCGGGTTAAATATCTCTGGGGATGCAACTGTCTGTG
GTTAATGGCTGTGTGAGGCCAGCGCTGGTGATAAAGGAATCAATCAAGA
CAATATTGAATTTAGAAAGGCAGATTTATTTAGAGAAAAGGAGAGATACG
TTGCAAGGGAGCAATGGGCAATACAGCAGAGGGAAGGCTGTCTGCAAAGA
GGCAAGGGCTACGTATGACGTAGGGCTGCTTAGGCTGAATGCTTGCAGAC
AAGATGCTTGCGTGCAGGTGGGCTGTGAGCTGAGTGCTTGGGTGCTAGTG
AGCCATTGGCAGCTGACCCTATTTCTTGGAACATTGCTCCCTGCAAGCA
TTTTAATGTTAAACCGCCAGGTCAGTTTGAATTTTCTTTTTTCTTTTTT
TTTTTTTTTTTTTGCTTTAGTAGGACCTGCCGTTGTGAGACTATCTGAGG
TAAATTAGACACCCTCCTGGTTTAAAGTCACCGCTCCAGTGACTAGGCAGG
GAGCTCTTCTTGAAGAGGGTGTGGGCAGTGGGTACTTTGCATGTTGTCC
ACACCAGGCGAGCTGCTGCTTACGGGCTTTGCATTTGCTCTTTTCTTTG
CCCAAAATGCACCTTCTCTCACTGTTTACATGATTTTTCTCCCTCTTTTCC
TTTTAGTCTTTGCTTAAATATCACCTTCTAGGGAGGCCTTCCCACACCAC
CTCTTCAAGATTTGAGGGTATGCACCCCCACCCCTAGCCTTCTTATCCCT
CTCCACTGCTTTCTTCTCAAAGCACTTGTTACGTTCAAATAAAATAGATT
AGTTACTTTATAGTTCTAATTTTACTATTTTTTGTCTTACTTCATCAATAC
CCATGTAATCTCTGGAAGGAACGTTTCTTTTTGTAGTGATTTCTAGCAC
CTAGAACAGTACTTTGGCACATGGCAGGTGTTCAAAGTATTGTTGATTA
TTTTCTCAAAGGGCATGGAGTCTTAGAAGTTTGAGAACACAGTTCTAAGC
ACAGCTGTTTAGAGACTATGGATGATGCTAATGGCTGTATTCCCAGTAGG
TGGGGCAATTCTCAAATTGACCTGGAATCCTTGAGATCTGGGGACAGTCA
CCAAGCACTGGGCTCTGTGGGGAGAGATGTGCTGGTTTTTAGAGAGGAGA
ATAGCATCCTGGGGGACTTGGCCCCAGGGCTTTCCTGTCCCAATCTCTTC
CCAAGTGAAGTCCCAGAGGCAGGAGGCCTTGTCTGTAGCTGGTCAGTCCTG
TAACTGTTTTCCCTCCCATCTACACAGATGCAAAGAAGGCTGAGAAAAGCA
AGCTGTGAGGTGAGCAGGGGCCCTGACTCCTCCCCAGAAGGCACTCAGAA
CTTCCATAGGGCAACTGGAAGAAGGTTCTACTTCTCACCAGCAGCTGT
TGCTGGGGGAAAAACCAGCCTCAGGCCCTACCCTGTGCTGAGAACCCTGAA
TCCAGTATCAGGTTCTCCAACAACTTGGATCCAGCTGACCCTCACAAGG
GGTCAGATGCAACCTTGTAGCATATGGAAAATGGCAGCAAGGTCCTTGTG
TGGACTATGCCTAGAATCTAAATTAAGACAAGGCCTCAGAGGGGCTAAGT
GACATCTGTCTCAAAGTTTACAGCTAGTGTGTGACTAAATCTTGATTC
CACCCTCTCAGGTTTTACCATAATCCCAAAAAGGTTGAAACAAGAAAAG
TTATCTTTGGGCAATTACCTCTTTCTGTTCTTCTTACCTACTAATGT
TCTAGGCTCACCTCTGGTCTGCAATCTCACTGAACTGACAGATCCCTCA
TGGCCTAAAGGGTTTTCACTGGGTTGACTAGGCTCTCCATTGCCTGT
CCTACTGTCTAAGGCACCTCCTGGGTAGGGTGCCAGCGTCATTCTGATG
CTGCCTGACTTTCCTTCCAGCTACTTTTGAACTTGGTATCCATGGCAGA

GGCTTAAAGGGCATGTTCCAGGTACTTTTATTTCCAAATTCCTCCAGTGGC
ATCAAGGAAATCAGCATCTCTGGATAGCTCTACTAAGGCTTAGTTCTCAT
TGTCCAATCTAGCTCCTGGGTCTATGGGAGGCATTACAGGAAATATTTGAGT
GTAAGAGTGAGTTGCTTTACCTCCAGAATATCCTTCCAATGGCTCTGAAG
CAGGCTGTGGAGTCTTGCTGGCTGATCACAGTTCACAGGTGGCTCCCAAA
CCTGTGGTCTACATCCATCCTTTGTCAAGTGTCACTGCCATTGTCCACAA
ATGTCATTTGGGCCTAGCCCCCTGGGATAGTAATCAGTCTTTACATAGATA
TACATTGTGCTTTACATCCACAGTAATTCTGAGTGGACCTTAAAATAAAT
TCCATGTCAGGTCTCACCAGCCCATGGGTACAGATGGGGTTACCTTTCA
GCCTTGTAAGGTGCCCCGTCTTTGAGTGTAGACATGGACTCACAACGAGT
CCACTCCTGCTGTTTCTCTGCTCTTGCTGAGGCTTCTGCTGCTGCTGCTG
CTGCTTTGCAGAGGCTGGCCAGCTGTGGTGCCTGAGGCACCTGTGTCTTC
ACAGCACCAACTTGCATGGTGGCCACGGTGTAGTTGGAAAGGGATGCTTA
GATGGGAGGCCAATGGGAGCTGCTTCAGGAGGCAAATCCAAGTCACAGAG
ATCGAGTCACCGAGAGCATAGTAACTCAAATCCCTTCTTCTGCTTAAT
AACTGAGATGCTGTCACTGGGTAACTCACCAGCCTTGTTTGTCTTC
ACTTAGATGATTTCTGTCTTAGAAGGCTCCTCATATCCTTCTGGGGAAG
GCTTCTAGTGGATCCACAGATAGCTGGACCAGGCATGTCCAGAAATAATC
TGATTCTCACATTTGAGTTAGCCAGCGTTCAGCTATATCCCCATTTTG
TGTCTATATAAGTTACCAAAGCCCACAAGGATATTAGGTGGCTCCTTAGT
TTGCTTTATGATTATGCCTTGTTGTGTGTGTGTGTGTGAGTGTGTACGCCT
ATGAGGATTCCTTCTCTCCCGTTCTTGCTATGGCTTCTCTCCCCACTGA
TGGGCTGTAGTTCCCTGTCCTTTTGACTTTGGGCTTAGTCATGTGACTTT
TTTGCCAAGGGAATGTGGGCAGAAGTAAGTGGGAGCCAGTCCCAAGCTAA
GGCCTTGGAAGCATGGTGAGCCTATGCCAGCTCCCTCAGAACTCCTTCC
CTTGCCATGAAGAGAGAATAACCTGGATTGTACCTTCAGCCCATGTCT
AGAATACAAACATGGAGAATAATGAACCTGACTCAAAGGCTGAAGGGCAG
CTGAGCCACATGAGGTCAATTGAACTGCAGCTACCTACAGACCTGAAAG
TGAAATAAACATGTATAAGTCTCTGACGTTTGGGGTTGTTTACATAGCA
TTATTGTAGCAGAAACTTAAATAAATACTGGGGGCTAAATATAGTGGACCA
GTGACAGCACAGAATGGTAAATGGAGTGATTGTTACTTACATCACAAACC
CTTCATCTCTGTTGATGGACACTAAAATCAAAGTGGCAATTACTCAGAGT
TGGGAGTCATTGAGTTGCATCATTGTTGTTTAGAATCATTGACAGTTTGA
GCTCTAAGTGATTACAGAGATGGTTTCTCAGCTACAGGTAAATAAACAA
AGGCACAGAGAAGTAAAGTGAATCTAGAGGGCTTCATTGATATTTAGCA
GCAGAATCAGAGCTAAACAATGAGTCTCTCATCTCCAGCCTTTCTATTCT
TGTTTCTAGGTTGGGATTTTGGGAAATAGTGCAGAGAGATTAGCAGTAG
TGACATGGAACAATGTGAGCCTCAGCTTCCATCCCTGAGGCTGCCTTCAT
CTGCCAGGGAATGTCTGTGTGCAGCCTTGCCCTCTGCACACAGTGTG
TATGGCCACCTGAATAAGTGTCTTTCTATAGCGACTAATGGATTGAAATG
GGTGCTAGAGCAGTGCTTCTAAAACTCCATGTATTAATCATCTAGGGGT
CTTACCAAAAACGCATGCAGATTCTGATTGAGTGGTCTGGAGTGGGGCT
TGACATTCTGCACTTGTAAACATGGACCACACTTTGAGTAGCAATGTAT
TAGATCATTCAGTGGAAACATGTATGAGTGATGGAATGAACAGATATAA
TTAATCCAGGTCTGGTAAGTGAAGTACTGATACATATTAAGTTGAAGTGA
ATTTACATCAAAAATAATGGTTACACAGTGAATTTTACTGCCCCCAAAT
TCTTTCTTTTGAAGTGGTTTCAAAGTGAATGAGCCAGCCAGGTTAAGTC
CCTGGTTTAGTGTGTGATTAGAAGATTTGATCCAGCTTTCTCCTCCTTCT
AATTCTTTAAATATGCAATGGCCTTCTAGAACTTGTCTCTCAGGCTCCC
CATGAGCCACCTGTCTTAATATCTTCCCCCAGGACATTTCTGGGTCA
AGGAAGGAATCAGGGACTAGGAAAAGTAGAAAGGTTGCCTGACAGTGAGA
AACTTTTTGCACTCCTATTTGTTCAATTCTAAATGTGGGTATTGTTGGG
GCTTCTAATTGGAATCTAACCTGAAATTCAGGCATGTCTAGCTATATATG
ACCAAGAATTAGGATGAGTTCAGTAGAAGCCTATTTTCAGGAGAGCGGTC
AGTTAAATTGAAGTTTATGGGTTTATGGTAATGGGTGGGGAGTTTACTT
CATTAGCAATAGCAACGTTTTTGAATCAGAGAAGTGATTTTGAACACACT
GTACATAGTTTTCTCACTTAGATTTATCTCTGGGTCAACCCTTGTTGGAC
CTATATTAGAATCATTTAGTGAAGAAAAGTGGGTGTCTTAGGAAAAGA
GCCATTTATTCAAATGTTCTGTTTGACATTAGGGCACTGGCAAGACTACA
GAATCAATAGATATTTAAAAACAGCCAGGTGCGGTGGCTCACGCCTGTAA

FIG. 4 (34 of 61)

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TCCAGCGCTGATTTCGC .TTACTTTGGGAGGCTGAAGCGGGTGGATTCT
 TGAGCTCAGGAATTC AAGACCCAGCGCTGGTCAACACGGTGAACCCCTATCT
 CTACTAAAATACAAAAAATTAGCCGGGCATGGTGGCAGGCGCCTATAATC
 CCAGCTACTTGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCAGGAGGCG
 GATGTTGTCATGAGCTGAGATCGCGCCATTGCACTCAAGCCAGGGCAAGA
 ATAACAAGACTCTGTCTCACAACAAACAAGCGAACATACGAAACAAACGT
 AACATCCAAACTAGCAGGTACATGCCGTGCCAGTCATGACCCATGGTCAT
 AAGATGTCTACAGCTCAGGAAGCAGCTGCACAATGCCTGCATAGACAAAC
 TCTTATGAAAGCAGAATGTCTGTATGTCTCCATAACACATAACAGTGTAT
 CCTTTTATTATGGTCATACACTTAGCTGTGATGTACCTACGCTCTAATATG
 GCAACGATAGTTTTCTTTTAAATCATCAACATAAAATGTCATGCTGTCA
 GTCCCCCACATGTAGACATAACTTAGCTGGTACATGGATAAGAAACCTAT
 ATTAGATAACCTTAGGCCAGGTGTGGTGGCTCATGCCTGTAATCCAGCA
 CTTTGGGGAGGCCGAAGCGGGTGGATCACGAGGTCAGGAGATCGAGACCA
 CCCTGGCTAACACAGTGAAACCCCGTCTCTACTAAAAATACAAAAA
 TTAACCGGGCATGGTGGCAGGCACCTGTGGTCCCAGCTACTCAGGAAGCT
 GAGGCGGGAGAATGGCGTGAACCCAGGAGGCGGAGGTTGCAGTAAGCCGA
 GATCACACCACTGCACTCCAGCCTGGGGGACAGAGCGCAAGATTTTCGTCT
 CCCAACCCAAAAANCNANNNNAAATTTGCACCCAAATCTGACTAATTCCA
 GAGCCAATTCCAATTAGAATCGTTATATCTCCCTGGTGAACCTGAAGCTT
 TTATCTTTAAGGAGACACACTCTTTATGTCTACCAATGCTTATTGECTTA
 AAGTCCACTTTGTGAGATACAGCTGCTTTCTTTTAAATAGTTTTTGTGTG
 GTATATCTCTTTCCATCCTTTTTCTTTTCCAGCCTTCTCCATTCTTACATTT
 TAGATATATTTCTTTTTCTTTTTTTTTTTGAGAGAGAGTCTCACTCTCTC
 GCCCAGGCTGGAGTAGTGCAATGGCGCGATCTTAGCTCACTGCAACCTCC
 ACCTCCTGGGTTCAAGCAATTCTCCTGCCTCAGCCTCCCAAGTAGCTGGG
 ATTACAGGAGCCACCACCAAGCCCAGCTAATTTGTTGTATTTTTTAGAAG
 AGATGAGGTTTCGCCATGTTGGCCAGGCTGGTCTCGAACTCCTGACCTCA
 GGTCACTCCACCACCTCGGCTTTCCCAAAGTGTTGGTATTACAGGCGCGA
 GCCACCATGCCAGCTGATTTTAGCTGTATCTCAAAAACAGCATGGGTTCT
 TGTTCGTTTTCTTTATTCAGCTTTTATAATGTAAATCATTTACATCAACA
 TCTAATACACCATGGACTGTAAAAACAGCCATATTTTATGTATGAATTA
 AAAAAAACCACCACCAATTAGTTCCTGAGACACACACCTTAAACAATAT
 CTCTGTGATGTGCATAAATCAATCACATCAGTTTCTCTGCACCTCAAAAT
 TTCTTTCTCAATTCTCAGAGATATGGCAATTTCTCTGGTTTTTACATTCC
 CAGAAGCAAAGAAAAAGTACACAGCTTCTTCAAGTCATGAGTAGCTTCTT
 TTTTATAGCTCTTGGTGTGTGCAAAAAAGATTGGAATTGCTTCACTAATA
 CTAAATTTTCATTCTGCTGCTCTGTTTCTATGACAAGTCAGAGGGCATCT
 TTTTGAAAGCATTCTAAACAGCAATTTAACTCAAAACATGTAATGACAA
 GACACACAAAATCAACTGATGACCAAAATGAAGAGTTCGACCAAGTTGA
 CACAAGCTGGCTGACAGAGCTTGTAATACACACAGCTTGGCATATGCCTC
 GCCATTTAGAGATGTAAAAATAGGAATAAATGTTTTCCCTTAAATCAAT
 GAAATAGAGCATTGGGACTGAAAATCTACGACAGTTATAGTGTTTTCTAT
 TCATTATTCTCATCTGTTTCTTCTCCCCCTTGCTTCTTTTAGTTTGAA
 TATTTTCTATCATTTCATTTTCTTCTCTACTAGTTTGAAACTTATGCATT
 TATTTTCTATTTTTTAGCACTTACCTAAAATTACTCTGTAATCCATGGAT
 CCTTAATTTATTAAAAACTAATGTTAATGAGTAGCTTTATTTTCTCTCC
 CATCTAATTTAAGGCCACAGAACACCTTCACTTACCTCAATCCTCTCCC
 AACTTACATGCTTTTAAATGTCATATATGTTAATACCGTATACCTTTTAAA
 CTTTCTAAAATAGCATTATTTTATAGCATGAGTGTTTCAATTTACATTTTG
 CATATATTTAGAATTTTCTTTGCTCTTCGTTTCTTCTTCTATTTATGACT
 CCCCTCTGGGATCATTTTCTTCTACTTGAAGTACATAGTTTAGAACTGC
 ACTATTCAATACAGTAGCCACTAGCCATGTGTAGCTATTGAAGTTTAAAC
 TAAGTAAAATTGAGTAATATTAAAAACTCAGTTCCTTCATCTCACTAGCC
 ACATTTCAAGTGCTCAGCAGCCACATGTGACTAATGACTACTGTACAGCA
 AACATATAGAACATTTCCATCATGGCAAAGAGCTCTATTGATAGTGTTCA
 TCCAGAGATTTCTGTTCCAGGACCAAACCTGAGGGTTGGGCTGCTATTTCTC
 ATGGCCCAATAACAAGATGAGCTGAGCTGGGGAGGAAGAGAGTTTTAT
 TTCTGCAACCACTTACAGGGAGAAGGCCTGGAAATCATCACCAGCCAAC
 TCAAAATTATGACGTTTTTCCAGAGCTTATATACCTTCTAAGCTATATGT

FIG. 4 (35 of 61)

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TACGTGTAAGTGTGCAT¹ACCTGAAGACGTAAGTGATTAACTTCTTTTAA
ATCTGTAACCTAAGGTCTGAGTCCGGAAGATCTTCCCCTGGAGCCTCAGTA
AATTTACTTAATCTAAATGGGTCCAGGTGCTGGGGTAATTACCCTTATCT
TGTCCCCTGCTAAATCATGGAGGTTTGGGGAATTCCTTTTAGAGCACCAT
TAACCTGTTTGTGAAGGCCTGGGAATTTCTCCAAACCCCATTAACC
TGTTTAAATCCCAATTGGTTCCGTTAAAAATTCCCTCCTTAATTTGTCCA
ATTTTAAAGGCCCAAAAAGGCTGGGGCAAACCTGAATGGCCTTTGTT
ACATTCCAACCTTTGTTTAAAAACACCGGTTTTTAATATTTAACTTAACC
ATTTAATCTCTACTGAAACACTTGTATATAAATCTGCATTAATGAGAAC
TGGCCTGCGCCATATCTCCTTCTCAGAATATCTTAGGGTTGTGATCCCCT
GTGTGAAGAGAATATATCTCTGGAGATCTCAATCTCTCTACCCCAAAAAA
AATCTCACTCGGAGAAAACCTCAGACTCTTATCTCCACAGCGCTATCTCTC
TCCTCTCC

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GCTTGTCTAAGATGGTGTCTCCTTGTGCTGTGCCTGCTTTCATCCTGGGA
TCTCCCTTACCATCAGGATTGCCTTCACCTCATTCCAGTCTTGGATCTT
TCTTCTTGTCTTCTGAGTATTTTTTTTTTTTTTGTCTGCATTCCCTTCA
GTGGCCTCTTGGGAAAAGATGTGTAGGGAGAAAAATTTTCTTTAGAACT
TGCATATCTGACAATATATTTATCCTATCCTGACATTTGGTAGATAGTTC
AGCTGGGTACAGAATTCTAATTAATTTTCTTCTGATTTATAAGACATT
GTCCCATTTTCTTCTGGCTTCCAATATTGCTGCTGAGAAGTCTGACACCA
TTCAAATGCCTGATTTTTTCCATGTGATTGTGTTTTCTGTCTGGAGTGT
TGTAGGATTGCCTCTTTATCTACAGTGTCTGAAATTTTATGACGTAGGT
CTTTCTTCATTCAATTATGGTAGACACTCAGTGGGCCATTTAATCGGGAAA
AACATGTGTTCTTCAAGTTCTACAACTTTATTACTTCTTTTCTTGTG
TCTTCTCTGGTCTGTTTTTCAAGCCCGAGTCTCTTAGATCTGTCCTCTAA
TATTCCTATTGACTTTACTTCATTTTCTAAGTCTTTATCCTTTTGCTTTA
CTTTCCGAGAGACCTGCTTAACCTTATCTCCCAACTCTTTTATTGAATTT
CATTTCTTTTACTATATATTTTTTACTTTGAATACACCTCTCTCTTCTC
ACATTTTCCCCATAGTATTTTGTCTTCAATTGACAGTTCTACTATCTTA
TTACTCTGGAGATATTAATAAGTTTTTTAAATTTTATTTATTTTATT
TTCAAAACAGTCTTTACTCTGTCACTCAGGCTGGAGTGCAGTGGTGTGA
TCATGGATCACTGCAGCCTTGATCTCTGAGCTCAAGCTATCCTCCTGCTT
CAGCCTCCCAAGTAGCTGGAACCAAGGCATGTGTACCATAACCCAGCTA
ATTTTTTTGTTTTTGAGGTGGAGTCTCACTCTGTAGCCCGGTCTGGAGTG
CAGTGGTGCAATCTGGGCTCACAGCAACCTCTGCCTCCTGGGTCTGGTT
CAAGCAATTCTCCTGCCTCAGCCTCCTGAGTAGCTGGGATTACAGAAACA
CACTACCATGCCAGCTAATTTTTGTATTTTTGTAGAGACAGGTTTCACC
ATGTTGGGCAGCCTGGGTCTGAACTCCTGACTTGTGATCTGCCCACTTGG
GCTCCCCAAAGTGTTGGGATTACAGGCGTGAGCCACTGCACCCGGCCACT
AATTTTTAAATGTGTAATAAGACGAGGTCTTGCTATGTTGCCAGTATG
GTCTTGAACCTCGTGGGCTTAAGTAATCTTCTGCCTCAGCCTCCCAAGTG
TTGGGATTACAGGTGTGAGCCACTGAATCTGACATTTTTTAAAAGTTTTC
TTCTCTTTACCAAGTCTTTTTTCCCCTTCTGCTTTTTTGGGTGTTTTTA
TTTTGATCTCTATCTTGCTAGAACTTTCTGCAGACGTTTAGTAATACTA
GATTTTTGAGAGTGGGCAACTGGAAAGCTGATTGGAACTCTGAATACAT
GGGTGAGGCTTGTGCTGTGAGTGTCAATTGCTTGATGTCTTGCAAGGC
CAATGGGTTTGGGACCCCTACTATTAGTATAGGCCTGATTCCCTGGGAAA
GGCTCTTTTGATCTCCTGCCTGGAGGATAAAGCCTGGCTACCAGCCTTC
TGTGTGTAATGTGAGGGAGAAGGGCTGGAGTATTCACATCATGCTGAAT
CCTTTCATGATCATCTTGTTTTTAGTAATCTCCTACCTTAACTCTCTGT
CTTCTGCTAGTATGGGAAAGATGACCTGAAAATCTAACCATTATTTTTTC
CCCCATTAAATACATTTTTATGATTATTCAGAAGTTAAATAATTGTCTATGC
TGTCCTCCAAAAGACTGAATCAACTAGCAACAAATAAGAATTTTCTCAC
AGCTCTGCCAGCATTTTTAAAAGAATAGCTTTATTGAGCCAGGAGGTCAA
GGCTGCAGTGAGCTGTGATTACACCACTCTACCCAGCCTGGGTGACAGA
GCAAAACCCTGTCTCAAAAAGAAATTTAAGGAACAGCTTTATTGTTGTA
AAATAGACATACAATAAACAGAGCACATATTTAAATTGTGCAACTTATAC
TTTGATATAACCCTGTGAAAACATCACCACAATCAAGATAGTGAATATAT
TTATCACCTCCTGATACAGTTTAGCTCTGTGTCCCCACCTAAGTCTCATG

FIG. 4 (36 of 61)

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TTGAATTGTAATCCCCAATGCTGGGGGAGGGGCTTTGTGGGAGGTGATG
AATTGTGGGGGTGCACTTCCCCCTTGCTGTTCTTGAGATAGTGAATGAGC
TCTCATGAGCTCCCCTTCACTCACTCTCTTCTGCTGCCATGTGAGGAT
GTGCTTGCCTCTTCTTTGCCCTTCTGCCATGATGTGTTTCTGAGTCCTC
CCTAACCATGCCTCCTGTACAGCTTGCAGAACTGTGAGTCAGTTAAATCT
CTTTTCTTCATAAAATTACCCAGTCTCAGGTGGCTCTTTATAGCAGTGTGA
AAAGGAACTAATATACCTCCTAAGTTACCTCAAGCTTCTTCTTAATTCCT
TCTCCTCCCTTCCTTCATTGCCAAGCAAACAACCACCTGTTTTCTGTCAC
TATAGATTAGTTTACATTTTGTGGGTTTTTTTTTTTTTTTGTAGACAAGGTC
TCACTCTGTTGCCCAGGATGGAGTGCAGTGGTGGCATCATAGCTCATTGC
AGCCTTGAACCTCTAGTTTCAAGTGGTCTCCCACTTCAGCCTCCTGAGT
ACCTGGGACTACAGGGGTACACCACCACAACCTGGCTTAAAAAATTTTTTA
AATAAAAATGGGGTCTTGTTATGTTTCTCAGGCTGGTCTCGAACTCCTCG
CCTCAAGCAGCCCTCCCTCCTTGGCCTCCCAAATGTTGGGATTACAGGC
ATGAGTCATGACTCCTGGCCTAGTTTACATTTTCTAGAGTTTGTATAAA
TGGAACATACAGAATGTATTTTTTGGCGAGTGGGGAGTGTCTATT
TCTTTCTTTCTTTTTCTTTTTTTTTTTTTTTTTTTTGTAGACGGAGTCTCG
CTCTGTCTGTTGCCCAGGCTGGAGTGCAGTGGTGGCATCTCGGCTCACCG
CAAGCTCCACCTCCCGGGTTCAAGCAATTCTCCTGCCTCAGCCTCCTGAG
TAGCTGGGACTACAGGCGCCCGCCACCACACCTGGCTAATTTTTTTTGT
TTTTTGGTAGAGACGGGGTTTCAACCATGTTAGCCAGGATGGTCTCGATCT
CCTGACCTCGTGATCTGCCCGCTTCGGCCTCCCTAAGTGCTGGGATTACA
GGCGTGAGCCACCGTGCCCGGCCCAAGTGTCTATTCTTAACCAGCTT
TCATGCAATCTTTTTTTATTTTACCATCTCTGTGATCCCACTCCCAAAGG
TACTAGATGTGATTGGTCTTAGGATCAGCTACCATTTGCCCCAAGTCT
TTCCAGCCTTCCAAAAATTTTTTCTTTTTTCTTAAAGATACTCCTGTG
TGAGGCTCAGAACTCTGAATTGCTACTGCAAAATATGAACTCGGTGATGT
GAATGCCAGGGAATTGCCTGATTGATCAAAGAAATGTATCCCTTCTCCC
TCACTCTTGCTGTCTTCTCATTGTGTTTTCCCATCCTTGTGGATTCTGTA
ATTTAAATATCCCTTTAATGTTATAATATTTAATGGCGTTTGCGAAAA
GTACAGAATTAGGTGCAAGAGTGATAGCTGTTATTTTTTTTTTTGGCCTC
TGAGACTGTTTATATATGCAAGTTATTTAACAGAAAGTTCTGCAGTGACC
TGAGATGTCAGGGGGTCTGATAGAGTACGTTTGAAGGCAGTTACTGGAA
AAAAATAATGCCATTTCTGGTTTGTACTTCGGTAAGTTCAGATGACCCAA
TATATTGTTTACATGTGGCATTCAAGTAAAAAAGTAGCTTCCCTCCCTTT
CTTCTTCTTTTCTCCTTTCTGCTTCTATAAAGCATCTGCTTTGGGAAA
CTTCTTAGGAGGAGAGCTTGCCAGCCCGTGGGTAATGGAGAGGTCTTGCA
GAGATAAAAGAGATGCTCCCACTCAATGCAGGATGGTGTGGAGGTAAATG
GGGATACGTCTGGCATCACTCAGGAATGGGCCCTTCTGGCAGGGAAGAGA
AGGGAGGGGAAAGAGGAAGGGAGTCAAAGATGAATTGCTGAATACGGGGA
TTCCAGGGCCTGGAGCCAGGAAGAGAACTTTGGGAGGTGTGAACCTGGAG
GGCATCAGCTGATGAGGAGCAGCCTGAAGTCCGGGGAGGACCTGTTTTTG
GTGGCCAGGAAGAAAGTGCCTTCCACACACAGGGAGGCCACAAGGCTGAT
GGGCTGGGGGTGGAAGGACAGCCCTAGGACAGGCTTGGGAAGCAGGCTC
AGGTAGGGACTGCGAGGTCTTGTGAGTCTTTTTTCTTCTGCTTCTAG
AAAATAGAATCCAAGGCCTCTTGAGAGTGGAAGGTGGGTGGGAGGAGGG
CAGATGGGGCTTAGGCCCAGGACACCCGTAGAGCTACTGCCAGCTGTCT
CTCAGGGACTCTGCTGAGGTCACTCCAAGGATCATTCTTAGCCTTGCTAG
ACAGTACTGACAGAGGGAACCGTAGTATCGCACCCACTTCTTCTCTTTC
AATGAAAGTTTAAAGGTCAACATTTCTCTGGCAAAGGAAGTTCCACAAA
TATTCATTTCCGGTCTTAGAAACAGCAAGGTATCAAGCAATTGCAAACT
TCCTGTGCTGGGGAATTCCAAGGAAGTAGGGGCAGAGTTCTGGTGGAGA
CAAAGTGAATTCAGAGTGATTAGTCAGTAGCAGTAGCAGTAGCAGTAGCA
GTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGTAGCAGC
AGCAGAAACCAGAAATTTCCCGCACGTGTCTCAGGCTCTCATTGCCAAC
CAGTCTCTAAGTATTTTTATTGGCAGGAAAAATAAAATAGCTATGAGTGA
AATAATTCATTAGACCTGAGCCTCCATCAATTTTGTGTTTAAAGGCCTGA
CTCTCTTTACCTTTCCCTGGGATGGAAGATGCAATGTTCTGATGTCAC
TGTCAAAAAAGAAGAACCAGTGGGTATATTGTATGCTTGAAGTCCAGCCA
TTTGTACAAATAGATAGAGATGACTGCCATGTGTGTAGACTTTCTATAGA

FIG. 4 (37 f 61)

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CTGTGTGCTAAACCCGACCTGCCACTTCCAAGGAGTAGATGAGGAATG.C
CATGGTTCTGGGGAGCCCTACCCCAATTTGGGGCAGACATTCCAAAGCTC
ATTTTCTGTGGAGGGGGTTGATGGTTAAAGGACGGCCTGGGAGTAACTCG
TCTGTACTAGGGCCAGGAGAGTTACATGCTGCTTCCCATGTTATTTCATC
ATCCCCCATGTGAATAGCTATGGCGTGAGGTCCAAGGTTAGGGCCTTTC
TACCATAAATGGGGGAATAAAATTCCCCTACCAGCCTGAGAAGTTTCTGT
TATAAAGAGGCTTTTTTTTTTGCGGGGGTGGGGGAGCAAGCCGACTAATGT
GTTATTTCCATACGGTTTGTTTTAAATGTAGATGTCATATGCAGGAGAG
GTGGTGTAGTGAGTCACAACGGGATTAGAAGGACCAGTCCGAAAAGCAGA
AGAGGGTCAAGTTCAGGGCACTGAGGACTACTGCATTCAAGTGGCGTGAAA
GGCAGATGGCTGAACAGGAGGGGGACATTACATTGCTTGTCTCCTTGAG
CCTCGATTTCTCATCTAAAAAGAGGGTCATTTATTACAGAACATTTAT
TAAACTTGTGCCAGGCACCGTGCCAGGAGCTGGACTAAAAATTAAATCCA
CCCCTGTGAGCTGCTCTGAAGGCTAAAATATGAAGTATGTAAAAGTAACC
AAGTGCTGTACACATGCAGCTATTCAATGACTGTGTGGGCATTGCGGCAG
ATTTTAATTTTCTTTTTTATTTCTTTCTTTAGTGAGAGGEGTTGGTTG
TTATTATTGTCGTCGCTGTAACGTCTATTTCACTTGCTTTTTTGTGGC
TCCAGCCCATTCAGGGCTGTCATCTAAGACACTTCTTATCACCTAAATA
ACCGGGGAGGCAAAGCGCTTCTTAAGAGATGGATCCAGAAGAACAATGC
TGGTTTTCTGTAGAAAAAGGGCTGTGGGAAGTAGAGATAAGAAGGGAAT
TGGCCAAGATGAATGTACAGAGCCTTATTTTTTTTTTATAACACAGCAAG
ATTAGATACAAAACAGGACAATAGCATCATCTGTTTTTATAACTGGAAAG
GACCTCACTTTACAGGTGGGGAAGAATAGAGTGGAGAAGTGAAGAGAATG
GTCACAGAGTCAATCAGCATGTCTGCGTCAAAGCTGGGATTCCCAATTCA
GGGCTCTTACTACAGTGACGTATGGCTAATATTTTGGCATTGTTTCGGGG
AAAAGCTGAAGCCCTGATGGTGTACGTCACTCTTGAGATAGTCTGTAGTC
CAGCAGGGAGGAAAGCAAGGAAGGGAGGTGGAGGCAGCATTTTTGGGTGT
AACATTTCTGTTCTTGTTTTGTGGCCAAATCATAGTGTGATTGGGACAAGC
CACTGCCTTTCTGAGCCTCCACTTTCTTTTTCTTCTTAAGAGGGAGGG
AATAGTAGAGTAAAGTAGTCATTTTATCAAACACCTGCTATTTTGGAGC
CATATTGCAAGTGGGTGGGGGTTGAACACTTGGCTTTATTACCCATAGG
ATTAAATCCAACCTCGATACTGTGGCATTCCCAAACCTCCAGTCTAATCTT
CTTCTCCATCAGCCATGCCCCACGACACCCTGGTCATATCTGATGTTGCC
CCTTGCACTTGCCCCCTCCTTATCTTTGCTTTCTGACCTACCATATGGCT
ATTGGTTGAAATTCTCATTTTCCAGGGCCTTGCTTAAATATCATCTCATC
CATTAAACCTTTCTTGAACCTCCCCTTGCCCTGTTCCCTCCCTAATGTCTC
AAGCCAGAATTTATTTCTTTTGTGGCCAAGGGACTGGGTTTGTGACCTC
TCTCACGAGACTTAATATTGAGACCAAACGTCTTTAGACCTCACCAGCCA
GAGAGATGAGCATCTATGGAATGCAGGCTTTTGCTGGACTTGCTGATGC
AGGGCCTCTGCCTTCTCCAGGGCCTCTCCTGCTGTTTTAGGAATTTCCC
TCATGGCAGCAGTCCATGAGCTCAGGGTCAAGTTCATACATGTTTTTACTT
CTTCTACTCTGCAAATGGTCTTCTTGAACCTCTGAGGGTCTTAAAGCTGCT
CTGCAGTTTGTGGGGTGAGTAGAAAGGGGCTTTCAAAGTTGTGCTGTTG
TTTCCCAACCCCAATAGCATGAAACACAAAGATGCTTACAAATAGCTGCCT
TGCTTTCTAGTCCCAACTTCTCTCTCCTGAGGCTTTAAACAAGTCCCC
AGGTTGAGCTGGACTGGAGTTGTATCTTATCTTCAATTATCTGTCTACTCT
CTTTCTGCTCTCTAGAGAAGATATTATATATGTGTGTATGTATGTGTAA
TATATAATATCCATATATAGAACATATATTGTTATATTTACATATACATA
CATAACATATGCATGTATTATATATACATATGTAGTATCAAAGTTGGAA
TTAAACTGTATATTTTGTAAATTTGCTTTTATTTGCATCTATCACTGTAA
ATGAATATTTTCCATACCGTAAGATATTCTTCAATGTATTTTTTTTTTT
TTTGAACAGGGTCTTGTCTTGTGTTGCCCAGGCTGGAGTGCAATGACCCGA
TCTTGGGTCACTGCAGCCTTGACCTCCCCGGCTCAAGTGATCTTCCCACC
TTAGCCCTCTGAGTAGCTGGGACTAAAGGTGTGTGCCTCCACACCCAGCT
TTTTAATTTTTTTTTGTATTTTTTTTTTAAAGACAGGGTTTTGCCACATTG
CCCAAGCTGGTCTTGAGCTCCTGGGTCCAAGCAATCCTCCCACTTTGGCC
TCCCAAAGTGCTAAGATTACAAGCATGAGCCACCACACCTGGCCTCAATG
TAATTTTAAATGGCTGTATAGTATTCCATCATGTGGTTGTACCCAAAATT
ATTTAACCAGTCCCCAGTTTATTTCAATTTTTTTTTTACTATTTTGAATAA
TGTTTTAGTAAATACCCACAAAATATGTACAATGGCTGGGCTTAGTGGCT

FIG. 4 (38 f 61)

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CACCCCTGTAATCCCAA₁ACTTTGGGAGTCTGAGGCAGGTGGGT₂CACCT₃G
AGGTCAGGAGTTTCGAGACCATCTTGGTTAACATGGTGAAACCCCGTCTCT
ACCAAAAATACAAAATTAGCCGGGTGTGGTGGCACACACCTGTAATCGC
AGCTACTTGGGAGGCTGAAGTAGGAAAATCACTTGAACCTAGGAGGCGGA
GGTTGCAGTGAGCCGAGATCACACTACTGTACTCCAGCATGGGCAACAGT
GAGACTCCATCTCAAAAAAAAAAAAAAAAAAAAAAGTACAATTTGTTG
TACCTCCCTGATTATTTCTTTTAAGTAGAATTTTCTTATAATTTT₄TTTA
TAAGTAAAATTTTGAATCAAGGGAGAAGCACCTGGAGTCCTTCAGATACC
TATTGCCAAACTGAACTTTTCTGTTCCAGGTTTACTACATTTCAGCCTGAC
TCAGGGTTTGGGGAGTAGAGGAGGGGGTGGAGGCAGAGGGCCTCTCCCTG
TCCCCACAGACCTCCCTTGGTGAGGTCCAAGTCTGGACAGGTGGAGTGTG
GCATTGCACCGTCAGGTCCCTGCTTCTGTAATTCCTTAAATCCATCCAG
TGGAGCCTCATTGTTCAAGTCTTTT₅TTTTTTTTTTTTTTTAACTCCC
CTGAAGACGGAGTCTCACTCTGTGCGCCAGGCTGGAGTGCAGTGGCACGA
TCTTGACTCATTTC₆AACCTCTGCCTCCCAGGTTCAAGTAATTCTCCTGCC
TCAGCCTCCTGAGTAGCTGGCACTACAGGCGTGTACCATCACGCCCCGGCT
AATTTTTTTTGTATTTT₇TAGTAGAGACGGGGTTTACCATGTTGGCCAG
GCTGGTCTCGAAGCTCTAACCTTGTGATCTACCCGCTCTGCCTCCCAA
GTGCTGGGCTTACAGGTGTGAGCCACCAGGCTGGCCTCAAGTCTATTTT
TTAACTCCAGGAGGCTGGTATT₈CAGAGGGATTAGGGCTGGCAGAAGGGC
CTCAAAGCTTTCAAGGCTGGGGAATAGGCTGCAGCCTGGTTCAGGGTAA
CCCAAGTGATTTTGGTTCCAAAGGGACAGGAAAAAAGTGATTGATATGG
AAGTTGTCAAAGTGCAACTGTCAAGACATTAAAAAATGTAACCTTTTAC
TAATATACAGTAGACTTGTGTTAAATATTTAACTGATTGTAAAAGGAAAA
AACCAGACGCAGTTTTCCCTACCATCTGTCAACACCTCAACACTGAG
TTCTTCTGTGACCTCTAGTCACCGAAATGCTTGGGGATTTCTCCCACCAC
TAGTCCTCCAGCAGCCGACACCAGTTGGGTGTCTAATTCACCTCCAACAC
TATCTACCTGGAGTTAGCGTTAGATCCACAGGTTGAGGGCTCAGTCTCA
CAAGACTGCCTCCCACTTCAGGTGCCAGTTACAAGTGGTAGGTTGTCCACC
TATGCTTCTGACTGATGGCTATAAATCTGGGTTT₉GCTTCCCTCGGGTTCC
GTGAATTTGCTAGAGCAGCTCACAGAACTCAGGAAAACACTTAAGTTTAC
CAGTTTATTCTAAAAGATATTACAAAGGATACAGATGAACACCAGATGAA
GAGATGCGCAGAGCAAAGCATGTGAGAAGGGGTGTGGAGCTTCCATGCCC
CTCTGGGGCACCACCCTCCAGGAACCTTCATGTGTCCAGCTATCTGGGAG
CCCTTCCAAACCTGTCTTTTGGGTTTTTAAGAGTGGCTTTATTACAT
ACACATGATTGACCGAACCATTGGCCATTGGTGACTGACACAACCTTCAG
CCCCCTCCACTCCCTCCAGTGGTTGGGGAGTGGGGCTAACAGTCTCAAGTC
TCCAATCCTGCCTTGGTCTTTCTGTGACAAACCCCATCATGAAGCTACT
GCATTGGGCTGCCAGCCAGCAGTCATCTATTAGCATGCAAAAGACACTC
TTATTATTCCAGAGATTCCAAGGGTTTTTAAAGCTGTATGT₁₀CAGGAAAC
AGGAGATGAAGAACAATATATATTTCAACATCACACTCGTTGGGGGA
ATTGACAGGATAGCAAACTGATTAAAGGAGGATAGGAGAGACTGAGATA
TATATTTCCATATATATATATAGAGAGAGAGAGATATTTCCATATATA
TATATAGATCTAGAGAGAGAGAGATAGAGAGAGAAGAGTCTTTCC

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ACACATTTGGGGGAGCAGTTCCGGAGGTACAGCCCGGACAGGAGATGTGA
GAAGATCGTGGTTANTGTTCCCCTGGTCCAGAACCCCTCCAAGTGGGCTT
AAGTAGGAAGGGTGGTGAGCGGCAGGTAAACACACGTCAAAGGCAGTCTT
CCTCTCTGAGGGAAAACACTTGTATAAGCATTGCAATCAATGGGCCTCTT
TAATTATGTCCAGTGGCAAGAGCGGGTGTGAACCCAGGGGCTGCCTC
AATCCGGGGCCTTTGAGGCAGAATAAAGTGGTCTCAGGTTGTTGGCATT
CCTTGCCCTTCCACCCGAAGCAGACACAAATCCTCTCTGGAGGCAAGTTC
CCCAATTCAGCCAGTACAACCTCCACAGACTAAGATCAATCATGTACAAG
CTCACAGACAAAGGTACCAAACACACAGAGCAATAAACAAATTCATGAG
TGACGTGAATGAGAATAAACAGAAACAATAACCACCAGCTGGGATGCTCT
AAGTCTTCAGCTGTTAGAATTCCTGAATATAGAATAAACTGCCACAATG
GCAACATGCATCTAGTACTTACTGTGTGCTGGGTTCTAAGAATTTTGCA
CATTGTGCCAGATACCGACTCAGCTTCACACTCACCTCCTACTGTGCCC
TCTTAATTTGCACTAGATTAAAAGGTAGAAAGGAAGAGGCAGCTATTCTG
TTCTTGGCTGTGCCTCTGGCAGCACATGCAAAATGGGCAGTAACAGTGGC

FIG. 4 (39 of 61)

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AGTCACAGGTAAGTAGC TTCTCACAGTGGAGTTAAAGGCATGGGAC
GAGACGAGCAAGGTTCTTAAAGGGACAGTGGCCAGTAAATGACCAGGGGC
TACTGGAGTGGCTGCATGGCTCTGTGGAAGCTCAGAGGAGCCTTGGGTCC
TGCAGGTGCAGTAGCAGCTTTCTGTAGTTCTTGATCTCTGGGTCCACAA
TCTTCCCCGTTTTTGTCTCCTCCACTTCTAATTTTGTAACTGACTTCCCTG
TGTGTACTTCTCTCTCTGATTGAAATAGCCAGACTGGTTTCTGTTTCCTG
ATAAGACATTGTCTGGTACGAACACAGTAACTCATTTAATCCGATATCTC
TATGAAGGAGGTACAATAATTATTCCTATTTTACAGATGAGGAAACACAG
CAGAAAAATAAAGTCAATTGTCTAAGGTTGCACATTTAGTCAAGGGAAGG
GTTGATATAACATATAATTATTTAGAAAACATCTAAGGAAATAAAAGGCA
TAATTTAAAAATAAACTAGGCAGGTTTAAAAAATGAAGTAATCTATAA
GTAAAAAAGTATAATTGTTGAAATACATATCTTAGTGGATGGGTAAATA
GCTGAAGAAATGATTAATGAACTGGAAGGTAGTTCTGAGGAAATCAGAAT
TCAGCATAGATAGAAAAAATGGGAATTTACAAAAGTACACAGGAATTATA
AAAGAGGTTAAATTATAGGGAGGGTAGAATGAGAATTAACATTGGTCTAA
CTGGAATTTTGAAGAAGAGAATAGAGAGAATGAACAAGGCAATATTTAA
AGAGGTGGCTGAGAATTTTTCAGAACCAACACAACTATGACTTTACCAG
TAGAGAAAACAATGTACACTGAGGAGGATAAATAAATATACTATGAACAA
ATTGTAATAATAATACTCAACAAAGACAAAGAGAAGATCTTAAATCAGC
AAAAAAGAAAGTCAGACTTAGAAAGAAATGACAATGGCAGACTACTCAA
CAACAACAATGGAAACCAATTCAGTGAAACAGTATTTTCAAAATGCATA
TTAATCTATCTTTGAAGAATAAGGGTGAAAAGGGTGAAAATTGCTGCCT
TATACAAAATATCAACATTAACAAAAGTAATGAAGGTAATATAAAAATG
TTTTCAAATAAAACAAAACAGAGAGTTTACCACCAACAAGCATTCTTA
AATGGACTTTTAAATGCAGTTTTTGAAGAAGGAAAACAATTCCTAAGG
AAGGTCTGAGATGCAAAAAGGAATTATGAACAAAGAAATGTTAAAATTA
TAGGTGAATTAAAAAAAGTGCCTGCATAAATGATAAATGACAATGATG
CTATTAATAATGAGTTGATAAGGATAAAGAAAAGGACAGAATTAAAATAC
TAGAAAACAAGCATGCTGGAAAGGATTAGGAATTACTTGAAGGTAAAG
TTCTAGGGTCTCTTCTATCCTTCTAGAGGGGAGTCAATATATTAATTTTG
ACCGTCACTTACACAGTGAAAAACTTTAAGGATAACCATAAAAAAATAGA
AATAGAGAGTATAACTTCTGAAACAGTCAAGGGAAAAATATGGAATAAGA
AACTGACCAAAAAACATCTCAGTCAATCAAAAAAAGAAAAAGAAA
GAAAAGGTTCCGAAGGAGAAAAATCAAAGCATAGAAAAGCGGGACAAATA
GAAGTGGAAAAGAAAAGGTAGAAGAAACAGGTCCAGAAATATCACTGAT
GCACTAAATCACCATTAAAGATGAAAACAAATGAACAACATCAAAAAAT
TCTAGTGACTGTAGTAGTGCTGATCAGAATAGGCTCTAAGATAAGATGCA
TTATTGTGAGTCAACTTGTGATGATGAAAGGTTTAATTCACCAGAAAGAC
ACAATTATAAACTTGTAAATCAAATAGTTTTATTTTATTTACTTTATTTAT
TTATTTTTTTTTGAGACAGGATCTTGTTCTGTTGCTCAGGCTGGAGTGCAG
TGGCTTGATCTCAGCTCACTGCAGCCTCCACCTCTTGAGGCTCAAGCTTT
CTTCTGCCTTAGCCTCATGAGTAGCTGGGTCCACAGGCACACACCACCA
AGCCCTGCTAATTTTTGTATTTTTGTAGAGATGGGGTTTTACCATGTTA
CCAGGCTGGTCTCAAACCTCTGGGCTCAAGCGATCTGCCCCCTCGGCTT
CCCAAAGTGTGGGATTATAGGCGTGAGCCACGGTGCCTGGCCTCAAATA
ACTATTTAAGTGAAACAAAACCTAGTATGGCACTAATGAAAAATGTATAAA
TCCATAATCGCAGAGGGATTTCAACTTACTTCTTTTGGATTATGTAAAGGT
CAACAGACAAAAGACAATGACAAAACCTTAATGCAATGAACACTTTTGAT
TTAATGAACATATATTGGATATGTACCAAGAATTAGAGAATACATACTA
GTTTTGAGTTTATGCAGAACATTTACAAAAATTTAGTGGAAGCCTAAATT
ATAAAAAGTTGCTGTCAGTAGAATAACACACAAACCCCTGAGTCCGGAA
TTCAAAGCCCTCCACACTCTCCTCTACCTTTGCATCTTTATCCTCCACCA
CACTGCAGTGCATACTCTGGGCTACTACTCACTGTTCTTGATTCAAATTC
CATGTTCTGTGAGCTCAAATCATCTCTCTGCTGGAATAACTACTTTCAT
ACATATTTCTGCTATTGAATTCTTGTCTTAGCACCCCATCTACTCCAAGAC
GATGTCAGTTGGGGTTACTCCCTGTCCCATTTTCTTTGATTACACTTTT
TTTTTCTACTTCCATTATATTATGATCACATCTGTGCCACAGTTTTTGA
CTTTGTGCTGCTTTTACTCTTTTCTAGACCCCTGAGAGCTCCTGAAGGGT
TGGGTCAATTTCTTTTTTATTTGCTCATTCTCATGGCACAGTGAGTGCTT
AATAAATGGCTATTGACTGAAATTAACCTGTATCTAAATGGACATATTCC

FIG. 4 (40 of 61)

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ACTTCTGGGCCATTCAATCTTTCTTTCTATTGGAACCAGGAGATCGGGAA
CCATAACAAAGGTAAGGTTGTGCCATGTGAAAGAACATGGAACCTTCCCC
TGAGGGCCAAAAAGAGCAGGGAAAGGTGCAAAGACAAAATCTTCCATTT
TTAAACAATGTAAGAATGTGGTCCACCTCATGCTCAGGTGGGACTTTATC
ATGACGTTATTTTTGGGGACTTATAGCTGCATCATTTACCCCATATACAT
TTACCTTTAGTGTAGGGAACTGAGGACAGGAATTTTGTGATGCAGACTC
TTGCTAATGAGGCTAACACTTGGAGAATTTTATCATGCATTCAAGAAGC
TTGTTTACATTTCTTCATTAATACTTTAGTTGGTGGTTTAGCTTTAGTT
GTAGGCTTATCAGATATTTGGAGATATCTTCATAAACGATGGCTTTGGTT
TTAGAAGAGTTATTCTGAAGCTACTATTTCTGGCAATAATCAAACAGCAT
GGCCATTTGTTTTGTAAGGCCTTTCTAAATATGACGGTAAATCTACG
TGTGGAATAATGCTTATTCTTCTGTCTCTATAAATGTGAATCTAGTTTG
TCTTCAAATGAAATCAAGTGATTAAATGTAGTTTTCTAAGAAGATAAA
TGGAGCAAAGCACTCTGTGTTTACAGTGTGGAAATCACTCATCCCTCA
TAAACTGTCCCAACTGATCCTGACTCACATGAATGAATTAATAAGAG
TTAATAACATCAATTTACATTTTTAAAGACACTTTCCCATGTTTAGACT
ATTGGTTGAAAAGCTGGTAGGTGTACAATTTGTGGAGAGTTGGCTGTTT
TTGTCTGTCGTTGTTTGACGTATTTCAAAGCCATATCTAATTTTGTGCA
GAATGGTCTGAATTTCTACAAAATGTTGAGTTGTGTAGTGTGGAGAAGTA
CGGAGCCATTTACTGAAAGGCTGGGGGGAAATGACGAGACCCTGAGATAA
GGCAGTAGTGGTGGCAACAGAGTGGAAAGGAGGTAGTTGAGATATGTTCA
GAGTAGAATCAGAATGGACATAGTGAACAACTGGATGCAGGTGGGGGCTG
AGGAAGCAAAGTTGAGGATAATTCTGAGACTTCTAGGTTGATCCACTGAA
GTTACATTATTCAACACCACAAGGAACTAGGGGAATGAGAAGGCATACT
GGTTTGCTTTGGAGTGGAAAGGGCAGTGATGTAAGAGGAGTTAATGAGTTA
AAGTTTGATATGCCTGAACTTCAATTTGATATGTGCATCTGATATACCC
TTGGGGTGACCCTCCAGGCAATGGTTGAACATGTGTATTTCTTAGTAAT
GATAGGCATCACAGACTCACATCAGTAAGGAAGCAACAGCAAACCTTGATT
GGACGATATACCTGGAACCTCAGTACCCTATGACTGGAGCAAGTCTCTGTC
AGTGAAATGAGGATAAGAAGAACTTGACCTTGTTGGAATATGTTGTTAGG
AATATATGTGATGAACAACTAGGATACTTCTACAGGGCTCCACATGTA
GTAAGGGCTTTATAAATGCTTGATAAATATTATTGTTGTAATTTATTTC
AAAGTAAGATGCCACTGGAGGAATCTTTGGAACCCAAATTAATAACAAAT
AGGACTGGATGCAATGGCTCACACCTGTAATCCCAGCACTTTGGAAGGCC
AAGGCAGGAGGATCTCTTGAGCCCAGAAATCAAGACCAGCCTGGGTGAC
ACAGGGAGACCTTGATCTATGAAGAATTAATAAATAAACCAGATGTG
GTGGTGCACGCCTATAGTCCCTGCTGCTTGAGAGGCTGAGGTGGGAGGAT
TGCTTGAGCCCATGAGGTTGAGGCTGCAGTGAGCCATAATTGTGCCACCA
CACTCCAGACTGGGTGACAGAGTGAGACCCTATCTCAAATAAATAAATAA
ATAAATAAATAAATAAGTACAAACCAGCAAACACTAATCCTTTCTAGAGA
TTATTGAACTCTGGAGGGCAGATCTGAATGGAGCCAGCAGAGGGACCTAT
GGAGATCAGCCTGGCCCTGGACAGCACCAGGCAATGGGGTTGCTAGAGAG
GTAATGGGGTTGAACAGGGTTTAAGCCATGAGGTCTCAAGAATCCGTGAA
GACTCAGACTAATTTTTTTTTTTTTTGCATGAGGATTAGGTGTTCTTAGGA
ATTTCAATGAGAGCAGGGTTAATGAAGGAATGCAGGGTAGGAGAGCTGAG
GGAAGGCATCTGAGAGAGCCTGGCTTATGAATGGCTGCGTCAGTATGGCT
CACCTGCTTTCCTTGATCTACTTAGCAGATGATCCACCCAGGCCTCC
AGGGCCAAGGTCATTTCCACATAGTCATGGGCCCTTGAGGGCCTGGAGCA
GTGTAAGGAAGACAGAGTCTTAAGAAATTGCATTAACAGTCATGGTGCTT
GGCAAGTGTCGTCATCCTATGCCAAGCCTGATCTGAAGGGGTGCATGCTC
ATAGGTAGCTGCTGCCAAGATTACAGCAGCTTCTTCAATCCCAGATCCA
TGCTCTCCTATATTCAATTTTCCAGGGGTTCTGTCCTTCGACAGTGATG
AGATGCAGAATGACTTATTGAGTTATTCTCCTGATAGTTGCCAACTTTTC
CAAATGACAATGGGGCATGGAGCTTGAGAGTGGAATGAGGCCCTAGGGA
TAGCGTGCTTAGGAAAACACTCCAGCCTGATGTAATCTGGGGGTACAA
TGGCATTTTCATCATCAAGACTGATGTAAAGGGTGACTAGCAGTGAGTTG
GGGGTGACTCGCACTGGGGCTAGGTTTCTGATTCTGCCTAATCCAGACAG
AGCAGAAGCACTAGTGGGCTGGTAGAGGGCCTCCAGGGCCTCACTTAATG
TCCTGGAATAACAGCTCCAGATTGTTGGTTCACGTTCTGAGGACAAGCTT
GGGTACTACAGGATAGAGAGAGTGGTGGGAGATGCCGTGGCCTGCCCTGC

FIG. 4 (41 of 61)

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TGATGCCTGCCCTGCCATTCTCTGCGTGTGATGTCTCTGGGGCATCTTGCC
TTCCTTGGCCAGACCTGTAGTTCAGCTGAGGGCATGTGGAGGCCAAATGG
CTTCTTAGAGTGTACTTTCTTGAACAGCTCTGCTGGGAGAACTGGAGG
AGCTAGCTAGTCACGGTAACTGCAGCAGTCAAAGGATCGTCCCGGTGGAG
GTGGGGTGGAAAGGTAGAGAAAGAGAACATATAGCGTTTTCTTGAGAT
GTGTGGGCATGTCTAGAGGAAATACCCAATTCTGAGCCTTGAGCCCTC
CAGGAAACCTTGGAATATTAGGTTAGTTCATCCCCAAGGAAGTCTAAGAAT
TCTGGTCTCACCCATCTCCTTTAATTTCCACAATGATCCTACATGATATT
AAGGAACACGGGCCAGTAACCCCTCCAAGCAATGGATGTGGTGGTGAAGTT
TGACCTCATGATGGAGCGGAGGTGGTTTTGAAACCTAAGAATTTAATTTA
TTGTTTTCAAACCTGTTCTCCACTCAGCGTTATTAAAGCATACATAATTGAC
ACATAAAAATTGTATATGTCTACGGTGTACAATGTGATGTTTTCGATCTAT
GTATACATTGTGAAATGATTACAACAAGCTAAATAACATACCCATTCATC
GTGTTTTCAAAGGAATTAAGTCAAGCACAAAAGAGAGGTGCTGTTGAAGA
GTAGGGCTGCTCTATCTAAGTAGTATGTCTGGGGTGTCTGGATCAGGG
TCCTTTTGTGCTAGTAATAAACAGCCCTTCTGGGGCTGCTCεACTTTCC
CCACATTTTCTTCTGGAGCCTCCCTAAGAATTAGGACATGGCCACTTTCT
CTGCATAGGCTTCCTACTTCAACAAGGACAGGGCTTGTGCTGCCCCATGC
CACTTGAGTGTCCCTACAGCACAGAGCTGAGTGCACACTGGCTGAGTGAG
GAAATCCCCCAGATTAATCTTGGTTCTAAGCATCATGGCTGTATTTCA
CGTATATGAATTACAAATTACAGCATAGTCAATAAGGATTTTTGTGCTA
CAACTGGAATCCAGATTATGCAAATTGGATAGTATAATATTGAAATTC
TAGGACTTTTTATTAGTTTTTAAAAAATTATACAAGCTTAGAGTAAGAAAT
TAAACAGTGCAAAAGAATTCAGTGTGAAAAGTAAATGCTCTGTCTGTGC
TGAGAGACAGATATTGCAGCCAGATACTACTGGGGTCAATAGTTTTCTT
TAAGCATGCCATTTTGTGTTTATGGGACTTACAGCTCAAGAAGCTTGA
CACTAGGGTTGATCTCAGAAAATCATTGTTGCAGGTATTAGATATGACCG
TCTCATAAAGATACACACAGACACAGCGATTGGAGATATTCACTGGGG
CTTATGGGGCTGCTTGTCTTTCTGCTCTGTGCCTAAGTTGGGGCTCAGAGT
AGCCTGGCATCGGCTGTGGGGAGAATGCTGGCATGGGGTTAGCAGGAGCC
CACTTAACATGCTCCTAAGCCACCTGGAAGAGTCTTCAAGGAGACCAGAC
TCCAGAGGCCCTAAGGAAGGAAGGACTTTTGCCCGTTTTTAGGTATTCTA
GTCCAGAGTTTAGGGAGGAATGGTTTTGGCTTTGGGTCTGTGTGCCCTTT
ACCGAGTGGGATGGGATGTGCCCATGAGCTGTTGAGCTGGCTCTTGAGAG
AGACAGCAAAAGCGGGAATAAGAGGTGAGGAAGCTGTGTGGTTGTAGGAA
ATCCAGCAGAGGGCCTGGGGGTCAAAGTGGTCATGGTAGTGACGGTGG
AGGCTGAGGTGGTAGAAAATCAGAGGACAAACCCCATGGGCTGCTGGTGA
TCTGACCGAGCTCCTATGCTCTCCTGGTTTATTTAGGCTCTGTAGCAGC
AGATGATTGGCTGGTGTGAGAGCAGTGCACCTGCCATATCAGGCAATCCA
AGACAAGTCCAAGCTACGCTGGGAGGAAACCTGAAGGCAGCAGCAGGTAG
ACTGGCTGAAGACAGACAGGCAGGCAACTTGTCAATCAGATTTGTGTTTT
TAAGGACTTTTAACTGGGGAGCCCTCCATGACAGATCAGATGAGAGAGGA
ATCTGGGTCCGCCATGTGTCAAGCTACCAGAGGGTCCCATCGGTGCTTG
GATCTTCTTTTGAAGCTGGGTCTGAGGTTTTGCAGGTAGAGGGTGAGCTGGT
CAGAGGGACCTATTGCAGAGCTAACCACACCTTCCAGGAATGCAAGCA
CAAGCACCCACCGCGGGCAGGCGGGCAGGCACTTCTCCTTTTGCCACCA
GGACCTCACAGAGGCTGATCTGGCTCTGTGAGGTGGGAAAATGGGTGTGA
CTTAGTACATAGAGATAAAAGGCTTAGGAGGCCCCCTCCATCCTGTGACCC
TGTCCCCAGACCACAGGTGCCGGCAGGTGCTGCTATTTCAAGGCTGGGCC
TCAGTGCAAGCTTGTGGTTTTCTTGCCACCTGTGATGTCTCCCACTAAT
GAAGGGCTCTCCATCCTCTGTCTGCCTCTAGCAAGTGGAGGCTCTGGGC
CCTGGGCAAGACACAGGGGGAAATGCCATCTGTATTCCAAATATATTTCA
ATGTGACAGGAAAGCTGTCTTTAGAGCACAGC

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GCATGTGCTCTACATTGATCCAGGAGTTTGAGACAACATTGCAAGACTG
GGCAACAAGCAAGACTCTGTCTCTACAAAAAATAAAAAAATTAGTTGGG
CATGGTGGTACATGCCTGTGGTCCCAGCTACTCCTAAGTTGAAGAGGGAG
AATTGCTTGAGGCCAGGAGTTCAAGGCTGCAGTGAGCTATGATCACACCA
CTGCACTCTANCTGGGTGACAGAGCAAGACCCTGTCTCTAAAATAATAA
TCGTAATACATTTTTTTTTTAAAGTAAACAAAAAAGGTACACTTTCTCA

FIG. 4 (42 of 61)

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TACCAAAATAAATTCCAAATAAATTAAAGGCTTAAACATGAGAAAGTTAA
ACCATAAAATTACTAGAAGAAAATAAAAGCAAATATTTAGATAATCCTGG
GGATAAATTTCTTTGGAATGAATTTCTTAAAGATGAATCTCTAAAAGTGA
AATTACAGGGTTCAAAGGTCTTTCTTTGTCCTTTCTTTCCCTTTCCCT
CTCCCTTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCT
TTCTTTCTTTATCTTTCTTCTCCTTCCTTCCTTCCTTCCTTCCTTTCC
TGCTTGCTTGCTTTCTTTCTTTCTTCTCCTTCCTTCCTTTCTCTCCCTTTCT
TTCTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTT
CTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTT
TTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCT
TCTTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCT
TCTTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCT
AACAGTCGCATGAACATGGCTCACAGCAGCCTTGACCTCCTGGGTTCAG
CAATTCTCTGCCTCAGTCTCTCAAGTAGCTGAGACCACAGGCACCCACC
ACCAAACCTGGCTAATTTTTGTATTTTTAGTAGAGATGGGGTTTCACCAC
ATTGGCCAGGCTGGTCTTGAACCTCCTGACCTCAGGTGATCTGCCTGCCTT
GGCCTTCTGAAGTGCTGGGATTACAGGCTGGGCCTCTACGCCCTGGCCGAG
ACTACCTCTCTTTAACTGGATCTCTGAGCTCTGGGCAGAGCCCACCCTG
AATCCTGGTCTCCAAAAGGGAAAATTATTAGGAGGCTAGACCATATGAT
GCTTTTACAGTGCACCTTAAAAAAAGTTTGTTTTTTTTTTTAAAAGACATT
TCTACATGCTTAAACTACAATCTTCTTGAACCCCAAGAGTAGCTTCTG
TTGCAATAGCTAGTCAAAAATATAATAGTCAAAAAAATCAGGTAACACAA
CACAAACGCAAGCAGTTTAAAGAGCTGAAATGAACTTGCTGTTTACACTC
TAGGGATTCCATAAGGAAAAATAGAAGTTTCTCCCTAAAAGGGAGCCTGG
CACCTTCTCCATTTTCTTTAAGGAACCCAGGCTATTATAAACTATTTTA
GGGCTCTCATGCAGCAGACGGTGCAAGAGAAAGGAGAGACAGCAGAAGTA
AATGAAGAAAACAGAATCCAGTCAACAGAGAAGAAAAAACTTTTGCTCA
AAAAAAGGCAAGTTCTTAGGAAAGAAAAAAACATGAGGGCTATTTAA
ATACAAAGACGCATACATACACATGCACACATCTTGGATGTTAGCTTTTA
ATTAAGCTGACTTTTAACTATTGAGGTCTTTTAAATAAACTTTTAAAA
TCTTATTACGATATTTTCACTAGGACAAATTGCTGCTATTTTCACTTAC
CAAGTATCAAACCAGAAAAGGCTTGATTTAGGAACCAACCCAGGCTGTC
GTGGTAGGAAAAAAGGCAGAACGTTAGCTATGGAACCCACAGCATGGGGC
AACAGCCATTGCTCTTTTCACTATGGCCTGGCTAGCAAAAAGGTGGCCTTG
TTATGTAAATAAAGCCCGTTTGGTGGTCAAAATGAAACATCTTTTCTTTT
TTTTTTTCTTTTGCTGGCCGTTTTTTTCCCCCACCATACCACGTTTGTGT
GTGTGGGAGGGTGGGAATTTAGCCACTTCAGAGGCCTCATTTCCCATAAAT
TTGGAAATTTCTTTGGATTTGATCAAGTCAGATAGAGTAGGTCAAACCC
AATGGGAAAAAGACTGAAACAGCAATAAAAAACAGAAACAAACAGTTAAGC
AAAATGAATGATCACACAACCTTATATGATTACTGAGTGCTCTAATGGTAA
GGAGAAATTAAGACCAGCTGGTTGTTAACTTTAGCCAAGACAAAACCC
AATTCAGCTACTTACCTAGGGTTGGGTCTCAGGCTGAAGACCGCTCACTA
CCGTTCTAGAAGCAAGAAATAAACTTGAACCTCGTCTTACCTGTGTAGCA
GGACAAGCCCGCAGACAAAATCCCTCAGACACCAAATTAAGAAGGAAGGG
CTTTATTGGGCCTGGAGCTGCGGCAAGACTCACGTCTCAACCAACCGAGC
TCCCCGAGTGTGCAATTCCTGTCCCTTTTAAAGGGCTCACAACTCTAAGGC
GGTCCACATGAGAGAGTCTGTATAGATTGAGCAAGCAGGGGGTATGTGAC
TGGGGGCTGCATGCACCTGTAGTTAGAATGGAACAGAACATGACAGGGAT
CTTCACAGTGCTTTTCTTATGCAAATAACCGATTAGATCAGGGGTCGATC
TTTACCAGGCCAGGGTGTGTCACCGGGCTGTCTGCTTGTGGATTTTATT
TCTGCCTTTTAGTTATTACTTCTTTCTTTGGAGGCAGAAATTGGGCATAA
GACAAATAGAGGGGTGGTCTCCTCTCTTACCTGCGGGGAGTGAGCTCAA
CTCCTTAAAGGAGTTACCTGCCTTCCATCATCAGGGAAGCAGGAAATCTT
GCCTTCCCTTGTGGAAGCAAGTAAACTCAAAACAAACAAAGAAAAAAC
AGGGAGTTGTACAGCAAAATAAACTTTTGAATTTGACCAAAATTTGGGAG
ATCAGGAATTTCTGAAGGAGATGCTTTTACACCTCAGCAAAATTTGCTCTG
TTGGTTTGAGCCATAAAGTTAGCTCATGCTGGTACCAACACCAGTAGGA
GATTTGTCAAAGGTAAGAGGCATCTCCTCAGCAATCCCTTCGTGGTTAC
CAACATGTGAACCTTGGAAATCTGAGACAGGTCTCAGTTAATTTAGAAAG
TTTATTTTGCCACGGTTGAGGACACCCACCCATGACAGAGCATCAGGAGG
TCCTGACCACATGTGCTCAGGGTGGTCTGAGCACAGCTTGGTTTTACACA

FIG. 4 (43 of 61)

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TTT TAGGGAGACATGAGACATCAGTGAATATATGTAAGATGTACACTGGT
TCCCTCCAGAAAGGCAGAACTTGAAGCAGGGAGGGAGCTTCCAGGTC
ACAGGTAGGTGAGAGACAAACAATTGCATTCTTCTGAGTGTCTGATTAGC
CTTTCCAAAGGAGGCAATCAGATATGCATTATCACAGTGAGCAGAGGGG
TGACTTTGAATAGAATGGGAGGCAGGTTTGCCCTAAGCAGTCCCAGCTT
GACTTTTCCCTTTAGCTTAGTGATTTGGAGGCCCAAGATTTATTTTCCT
TCTACATCACTGTGGGCAGCTGACTAGGAAAGCTTTGTAGGACTGGTGGG
CAGTGTGAGAGCCCAGTGGGGGGTGGTGGTCCTGTGCCAATGGTAGCAAC
CACCTGTGAGGCTGAGTAACTCATTTCCTAACCTCCTCTAGCAGCCCCA
GTGGAGATACAGATGAAGCAGACTAGCGATACAACCCAGCCTGAAGTTTT
GTCTGGTGAGTGTAAATGGAATAAAAAATGGGAAGGGTGCTGAAGAGACCAG
CAAGAAAATGGTTGAAGAGATGGGGCACAGAAATTAAGCTGGATCAAAAA
GGACGGAAGCAGAAAGGGCCGATAGAGAGAGGGGATATCTATGGGTTC
GCGATTCTGAAAAGGACAAATCACTGGTGCTTTGAGAAGAGAGAGGGTGA
GAAAGCAGGAAGGCTGGAGGCTGTCATCCAAGAGGCGGACATCTGTGAAC
ATGATTCCAAGAGTCACCAGACCATGGGGGTGGCCAAAGGGAGTGCCTCT
TCTCACCTCCTACTCTTAATTCCTTGTACTCAAGATAATAAGTCCCAGA
AGAGAAGTACCCATATTTAATTCATCTGTGTCTTCCTAGCAGTACTAAAA
ATATTATATGAAAGGTATCAAACCTTTGAGAATGTGTGCTGCTAAATTGT
TAAGGATGCTGGAAAACCTCAAGACGTCCCTGATCCTGAGCCTGAGTATGA
GCCTGTGGTGAGGCCAATGCAGGTCTCCATTCAGACAAAGGCCTCAGGGA
ACGGATGAGACCTAGGGACAGAGATGCATGCTGGAGCAGCATCCCCATC
CCTACTGCAGCTCAGGCCAGCTGACTGCTTTATGAGTAAACGTTACCAGG
GAACACTTTGCAGTCTTAACACACATGCCCCACCTGTGACCACTGATCCCT
GTTGGGTGACCACTGACATCAGAGATTCGATGGCAGCAATGAAGACAAGG
CTATCCTCATTAGGAAGGAAAGGAAGGAGGAGGGAGGGCAAACGAAT
CTTTCCTGCTTGTCAACCACGTCCATCTCTGTTAGGTGATTTCCCATGTG
TGACTTTGTTTATCTTTATAATAACTCTGAGAGGTAGGTCTTGATGTCCA
CATTTTGAACATGAGGACATCCAGCCAGGAAGTTGAGTTCTGGGGACATA
GCTGAGAGGGCAAAGCTACATATAAACCCCTCTTTGTTTTTTCTGGCTTA
TCCACTGAGTGGCCCCCTGCAATCCACCAGCCCATTTGTGAAGTGCATACT
ATAGGTAAGTTGGGCACAGGAGGTGGATGTGGGCGATTTTGTACAGCT
CTCCAGGAACCTTACACACTGGTGAGGAGGGCCAGGTATGTTCTGACCAG
TCACAATCAAAGCAACCTCCTACTAATCAGGGAGGCTTGGTACCTGGGGA
ATGCTATGTTGAAAGGTTCTTTTCTGGGTTTTTAAATGATGGGTCTATTT
CCTTATTCTTAAGATTGCTTTTTTTCTGGCTAGAACTTAAAGAAATTTT
CAGTAAAATTTCCCTTCCCTGGCACAAAGTGAGCTTGAAATGAATTCCCA
GGTGGCCTTGATACTTTAAATATTGCCTCCTATAAAATCAACCTTTAGA
AGAAGGAAGTCAAAGAACATGCTAGATTTCACAAAGGTTAATTCCTTGAA
ATCCAGTTATCTACAGGACAATGTTGTCAAAGAAAAAATTATTTGGCCAG
GCACGGCGGCTCATGCCTATAATCCAGCACTTTGGGAGGCTGAGGCAGG
TGACTACCTGAGGTGAGGATTCGAGACCAGCCTGGCCAACATGGTGAA
ACCCCATCTCTACTAAAAATACAAAAAAATTAGCCAGGTGTGGTGGTGG
GCACCTGTAATCCAGCTACACGGGAGGCTGAGGCAGGAGAATCGCTTGA
ACCCGGGAGGAGGAAGTTGCAGTGAGCCAAGTTCAAGCCACTGCACCCCA
GCCTGGGCAACAGAGCAAGACTTTGTCTCAAAAAAAAAAAAAATTCAAT
GATATTTTAAATTCATGGTAAGGAAGATTTCAATCAGAACCAGCACAGA
AGATATAGGAAACACTGCAATGGGACTTTGCGGTGGGGGAGAGAGATTGA
ACACAACATACATACAGCACGGGCAAGGACATATTCATAGCCAGGAAGC
AGAGCAAAGATCAGTGGATGCGAAATTAAGAGGAAACATGAAAAATA
AGGGAGCTTCTGCCTAAACCCACCTAACCGGATCCTTGCTGAAGACAGGA
CAGGGTGATTGGACACCACTTTGGGGATGGTGGAGGATGGGGAATCCAGT
GAGATTTCAAGGGTGATCAGATATTGAACATAGAAGGTTCTTGCTAAAAA
AGGAGTTTACAAGAAAGTGACAAATGTGCTGGGAGAAGGTTTCAAGGAGC
CTGACTAAAATTTGGTCAAGCAGAGAATATTGCCAAGATAATAGCTAAG
TCTTCTGACAAACAATAGATGCTAAGCCAGCAAGGGTGATGTGCTCAGAG
AAAGCACTGAGGGCTTATTTCTTTTCCCCCAATCTCCACTCAGTCAAGT
CTAGTCCCCTTGTCAATGTAGCCATTTGTAAGAATGCAATCAGGCAGGGT
CCCATCTCCTAGTGACAGGACTGACTGAAGTTCTGCTGAAGAGAGTGGCC
TGGGGCTGACACCGAGATTTCAAGATCCTGGGTTTTGCGCGAGAGCTCAGT

FIG. 4 (44 f 61)

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GTAGTGCCATGCCCTCTCTCCACCTGAACGCCCAGTGTGGGCAGGAACAA
CTGCAGCTAGAAGTCTGGCACTTACGCTGGGGTCTAAGACCTGCCTGATC
TGCTAACTAGTCTTGTCCCTTGGCTATAAACTGACGTTGGCACCTGGCCA
GAAAGATGAGCAAGAGATCTCTGACACACCTTTAAGTCCCTGTGGAGTAG
GATTATGTTGGGGAAGGTCATTCTCTTGACTGAGCAGCAATTTGAGAAGG
AAGTCCCATGCCGAAGTGAGAGAAGGCAGGGAATCCTGCCTAGTCAGCTA
GAGCAAAACAGTCTGCAGGACGGGACCCAGGGATGTGATCCTCCCATCCA
AAGGCAGTGAACATAAATGACTAAAATACTTTCCAGGGCTCACGTTCTTTG
AAGAATGGGGACTAAAACTAAGACAGGAGCCAGCAAGTGAGGACTTGGAA
GGAGATGGCTCATCTGATCAGCCTCCACTCAACAATTTTAATCATCCACA
CTGGCATGGGGACACAATATGAATAAGTTGACAGGGACCTACTCTGATTA
AGCAGTGGGCTAGTGCAGAGACCTGTCAGTCAAGAGTGGACAGGAGATGA
TTTCAGACAGTGAGAACAAAATTAACAGAGTCATGTGCTAAAGGGTGGCT
GGAACACAGAGGAGTTTAAGACTCAAGAGGTCTGGCTGGGCGCGGTGGC
TCATGCCTGTAAATCCCAGCACTTTGGGAGGCGGAGGCGGGCGGATCACAA
GGTGAGGAGATCAAGACCATCCTGGCTAACGCAGTGAAACCGEATCTCTA
CTAAAAATACAAAATATTAGCCAGGCGTGGTGGCGGGCACCTGTAGTCCC
AGCTACTCGGGAGGCTGAGGCAAGAGAAATGGCGTGAAACCGGGAGGCAGA
GCTTGCACTGAGCCAAGATTGCGCCACTGCCCTCCAGCCTGGGCGACAGA
GCGAGACTCCGTCTCAAAAAAAAAAAAAAGACTTGAGGGAGTTGTTTATT
TTTGTCTCTTTTTAAGACAGGGTCTTTGTTGGGCGCGGTAGCTCACGCC
TGTAAGTCCCAGCACTTTGGAAGGCTGAGGTGGAAGATCTCTTGAGCCCA
GGAGTTTGAGGCCACTCTGGGCAACATAGCAAGACACCGTCTCTACAAAA
AATGTGCAGGTTGAGGCTGCAGTGAGCAGAAAAACACCGTGCCTCTAG
CCTGGATGACAGAGCGAGACCTGTCTCGGAAAAAAAAAGAAAAAGACA
GGGTCTCGCTGTGTACACAGGCTGGAATGCAATGGTGCAATCATGGTTC
ACTACAGCCTGGAACCTCTGAGCTCAAGCAATTCTCTACCTTGGCCTAC
CAAAGTTCTAGGACTACAGGTGTGAGCCACCACAGTGGCCTCAGGAGAG
ATCTTAATAATAAAAGGACAAATTGCCTTGCAATCCCTTAGGGGCAGGATT
GACACATCCAAGGATCAGGCAGAAAGCCTGTGCGGAGTGGGATGAGCAAA
GAGAAAGGCTGAGAGTTGTGAAGAGGGAGATGCAGTGCCAGCTAGGACAG
GCCTTTTTGGGCTATGGGAGGTTTTTCAGAGGAGACCCACCTAAACTAAC
CCATAACATTGCAGTGGGGACCTGTTGAAGTCATGGACTACTACCTGAAA
GCCAGAGAAATGGGAGGAGCCTTTCTCTGAGGAGGGACTCTAGTCCATA
GGTATCTTGCCACCAATAACATGGACAGGCCCTGGGGGAAGATGGTGGTA
GCCCAGCTGGAGGAAAACCATTTGCCACCTGAACTAGCCCAGGGTAAGCC
ACCCAGGCACTGAGGGTGACACCCATGCATGCACACACAGAATCACACT
CCTTCCCTATTATCTCAATTGAGGGTCTCAACACCCATTTTTTTTGTGTT
TTTTGGGTTTTTTTTTACATGTTTACATTTTATTATTATTATTATTGTGA
CAGGGTCCCACTCTGTTGCCCAGGCTGGAGCACAGTGCAGTCTGTGCAATC
ATATTAGATTGGTGCAAAAGTAATCACGGTTTTTGTGCTTAAAGTTTTG
CCATTACTTTTTAATGATAAAAACACGATTACTTTTGACGCAACTTAAAA
GCTCACTGCAGCCTCAAATTCCTGGTCTCAGGGAATCCTCCTGCCTCAG
CTTCTGAATAGCTGGGACTACAGGCACATGCAATCCTACCTGGCTAATT
TTTTAAAAATTTTTTTGTAAAGATAGAAAGTCATTTGTTGTCCAGGCT
GGTTTCAAACCTCTGTCTTTGTGCCTCCCTCTGCCCTGTGCAAGACCTTC
TGGATGCCCACTAATGAAGACTTCCAGGGAGAGGAAAAGTAAACATAGGT
CCCTGATCAAGGGACCAGGGTTTATCGACCACAAACAGCATGCCAGATT
CCACTGGCAGTCTAGAGGTGCGATTTGCCCCAAGTGTGTGTGGAAGGCC
TCTCCCTAGCAGTTGGTTTATACACCAGCCACAGCACAGCATATTCTCTT
AAATTGTGAACATTTGCAAAAACCTCTTGAGGACAACTATCATGTCTTGT
GTACTTTTGTGTTTCCCTTCCCCTATGTACACGCGCGCGCATGCACT
CATGCACGCACGCGCGCGCACACACACACACACACCCCTCAAACCTGAA
TGCTTGGTGTGCTGAATGGATGAATGGCTAATGTAAGTCATTCTAAAGC
TACTTTCTTTGGCATACCATCACCTTTGATTTTCATCTTTCTGGAACCTCT
ATGTTCCAGATGAATTTGGAAAGCCCTCAGGAAACATTTCAAATTTGCT
ATATGGGAGAAATGGGAGGGTCTCTCTAGAAATTTACCTGCCACAGGTAT
TTCTGGTAAGACACAGCAAGGTGGCACCACCCATTCTCGTTACAATGT
CAATGCCAGTCACCTTCTGTCCCATAAAACCTTTATTAAAGGTGCAGAA
TCCCATGGAAGCAGGTGGACACCATCTGCTTCCAGCCAGCCAGGGGAGCA

FIG. 4 (45 of 61)

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AGGTGTCCACTGTGCCCTTGTGGCAGGAACTGCGCTTCTCTACTCTCCCA
CTTTGAGGCCTCTGGGGCTGGCCTGCTGCCTCCTCATTGACAAGGCTGCT
TACTGAGCAGTTCATTCTGAGCTGGACATAGTGCTTCTGGTGAGTCTCTA
CTTCTATTTAACCACAAAGATATTCTTTCTAAGGAAACGCTTTCCTGTGCG
GGGGAGGTTAGCTCCAGATGGAAGTCACAAGTGATGGCATGGTAGCTCTC
ATCCGTTTGGGTGGATGATATTCACGGAGCACCACCATGAGCCAGTCATG
GAGGTGAACAGTATATGCCAGCCCTGAATCAGGTGCATTGACAGCAAGGG
AGACAAGCAAACAAAGCTGAGGTTTGGCTGAGGATGTTCAAGACTCACACA
GCACAGAGGAGCATCCACCACCCAGCTTGGGAAAGGACTTGTTATAGAGG
GGGTGAAGCATGAGCTGAGTCTTGAAAGACTAGAAATTAGCCAAACTACA
AGGAGGAGAAGGAGTTTCCAGTCAGGAAGAACAGGTTATGCAAAAGCACA
GAGACTAGAAAGAATATCACATTCAAGGAAGTCAAATAGACAGGAAAGA
TTGATGCGTGAGGATAGGAGAGGAGGGCAGGGGATTCCAGGTGGGCCCTGC
TTGCCACACTCAGGAGCTTGAACCTATCCACAAAGGAGGTGTGGAACCAG
TAATGAATGGGTTTTGTGCAAGGGCTTCATGTCACCAGATTTGCTTTTTG
GAGATACTTCTGTGGCTGATATGTGAGGAAGGGATGGAGGAAGTTTCCGT
GGCAATCAGGAAAACCAATTAGCAGATGATTCAAATGGCCTAGGGGAAAA
GGGAGGAGGACTTGGACTACCATGCAGCAGCAGAAATGGAGAGAAATAAC
AGATCCCAGGCACCTCAGGAAGCGCTCAGAATGAGCCCTCAAAGAACTTA
TGGTAGGTGATGGATGGAGTGTGAGTCTTGGGATAGCATTGCCTGG
GAAAATACTTTCTAGTTGAGACAGGGAAGTGGGCCAGCAGAAATGGAGGG
CTTCTTCTTTTGTCTTAAATACTTTTATAATATTTGGAACCTTTGAAAAT
GAGCAGATATATTAGCAAAAAGCCTAAAAGGGATATTTTGAATCACTG
CTAGTTCTAACATATAACTTTAGCTTGCACACATCATCAATTAACCTTG
ATAGCGCCTTTCTGAAACTATCATCCCAAATAGCAATCCTTGTA AAAAACC
TATTTTGAAAAACGGGCCTTGTAGGATAGCCTCACAGATGTTTTGTGGTA
GATTTTCTAACATTCTAATGTGAGGGAGTGAAAGGAATCCCGTTAGAAAGT
TGGA AAAATCTGGAATCTCTATTTCATGGTATTAAAGTTTGCCGTCACAC
AAAAGTTTAACACCTTTACACAATCAGACTTCCTCATTTTACATTGCTCG
GTAATCCGGAATCAGTCACCCAGAGCCTGGGTCTTAGACTTGACAAA
ATGCATCCCAACAAATCCTGAGTGGCCTTGCTGAGGACTTCTCCAGAAGA
TAGAAAACCTCAGTTCCAGCCAACAAGGGGGAAGCAGCTGAAGAAGTGAAA
TTAACAAAGTCTGGAAGGAATGACCAATCATCTTTGATTGTGTAATA
ACCAGAGAGTAGAATACAGCTACGACAGACATTTTGGGAGAGAAGCATT
TATCATAGCTTTTGAAGAGAATATTTTTCAGCATCATAAGCACACAATT
CCAAGACAGATACTTTCAAGGGATTGTTTTGACG

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ATGTTNNGGTTTTGGGACCCCATTCAAACTTCATGTTGAATTTTAATCTT
CAATGTTGAGCGAGGTCTGTGGGAGGGTGATTGGATCATGGGGGTGGGT
TCTCCCTTGCTGTTCTCAATGATAGTGAGTGAGTTCTCACAAGACCTGGT
TATTTGAAAGTGTGTAGCACCTCTCCCTTCATTCTCTCACTCGTCACTG
CTCCGCCATAGTAAGATGTGTGTGTTCCCTTTGCTTCCGCCATGATT
GTAAGTTTCTGAAGCCTCCAGCTATGCTTCTGTACAGCCTGTAGAAC
TGTGAATCAGTTAGACCTCTTTTCTTCATAAATTACCCAGTCTCAGGTCA
TTCTTTATAGCAGTGTGAGAGTGGATGAATATAGTGCCATATGTTTGTAT
TCCAGCTACCCAGGAGGCTGAGGTAAGAGGATTGCTTGAGCCTGGGAGT
TTAAGGCTGCAGTGAGCCATGACTGTACCACTGCTCTCCAGCCTGGGTGA
CAGCGAGACCTTGTTTTCCAAAAA AAAAAACCCAAACTGTGTAAATGTG
TTCATAAAAGTGTCTTGCTCCACACCTGTCCCTATATATCTTATTCCTC
AGCCTCCGACAACCTACTTTATTCACTTCTTATGTATCTTCCAGAATCAAA
AAAAAAAATCAAATACAAGCAGTGAATGTATTGCCCTTCTTCCCT
CCCTTTTGTATCATCAGAGTTAGCATATCATAAATACGGTCTGCATTTTC
TTCTTTTTCAGCTATCAGCATGTTTTGGAGAGGATTTTCATATTCGTGCAG
ACAGCATGTATTAGTCAGTCCTTGCTTGTATAAGGAAATACCTGAGAC
TGCATAATTTATAAAGAAAAGAGGTTTAATTGGCTCACAGCTTCGCAGGC
TGTTCCACAGGAAGCATGGCAGCATCTGCTTCTGGGAGGCCTTAGGAAG
CTTTTACTCATGCAGAAGACAAAGCGGGAGTGGATGTCTTATATGGCAGG
AGCAGGACTGAGAGAGAGAGAGAGAGAGAGAAAGGATGCCACATACTTT
AAACAACCAGATCTTGTGGGAACCTGTGTACGAGAACAGCACCAAAGGGA
TAGTGCTAAACCATTACATAAGAACTCCACCCCATGATCCAATCACCCCA

CACCAGGCCCCACCTCCAACATCGGGGATTACAATTTGACATGAGATTG
GGCTGGGACACAGAACCAACAATACCAGAGTGCTTTCTCATTCTTTCT
ATAGCTGCCTAGTATTCTATGTCCTTTACTTCATTTAGGCAGTCTCTGT
TGATAGACACTTGGGTACTTCCAATTTTCTTATTACAAATGATGTGCA
ATGAATAATTTTGATCATTTCATTTACATGGGTATGTCCATCTGTG
GGATAAATCTCCAGGAGTGAAATTGCTGGATCAAAGGGGAAGTGCACCTG
TGATTTTCATAGTTAGCAAATTTTGTCTATAAGGGTCATATCAATTTAT
AGTCCCACGCGTAATATTTAACAGTGGGGATTCCCGACAGTTTGACCAA
CAAGGTCTGTTGTTAACTTTTGATTTTTGTCAATCTGATGGGAAAATAC
TAGTATCTCAAAGTGCTTTTAATTTGACTTTCTTATTACAATGTAAAGCA
TCATTTTACTCTGCCAAGATCAAATAGTATTTCTTTTCTGTGAACAGA
CTGTTAAGATCCCTTGCTCTTGTGTTTGTGCTGGATTTTGTCTTTTTTT
CAAATGTTTTGAGGCAGTTCTTTACATGTGAAACAAGTTATCTCTTTATC
TGGGGTGTGAGTTACAACACTACTTTTCTCTGGCTTGTGCGCTTTGAC
TTTGCTTCTGGTGATTCCCGCAATTCTGAAAGTGTACTTTTTGCATCATT
CATTCTTATACACCCATGCTCTTGTTACGCTGGTTCCTCTAECTGAGGG
CTTTTTCTTTCTTTCTATCTGGGAACATTTTTTAGAGACAGGGTCTCA
CTCTGTCATCCACGCTGGAGTGCAATGGTGGATCACAGCTCACTGCAGT
CTTGAACCTCTGGGCTCAAGCAATCCTCCAGTGTGAGCTTCCCAAGTAGC
TAGGACTACAGGTGCATGCCAGCATGCCTGGCTGATTGTTTTATTTATTT
ATTTATTTTTTTAGAGATGGGAGTCTCACTATGTTGCCCAGGCTGGTCT
TGAACCTCTGGGCTCAAGCGATCTTTCTGCCCTGCCACCCAAAGTGCTG
GGATTACAGGCGTAAGCCACCATGCCCAGCCCATGTGTGGAAATCTTCTG
TTTATCCCTTTAGGCTTGATTCTTATGTCGTTCTCCTCCCTCCTTCTGG
CTACTCCTCTTGTTCTTTATCTTACTCTACTTGTGATGTTACCTTGTTTC
TGCTTATAACTAGCTGCCTCTCCTATCTGAGGAGGGACTTGTGACTGTTT
TCATCTCTGTACTCCAGGTCTTAGTACATAGCGCTTGCTCAACAGATGT
TTGGTGCAATTGATAGATAAATCAATGGTAGCTGTTAATACCAGTCCTGAC
TCCCTGCAGTGCTTCAGCTGATCCTGTTCCAGATGTGCACTGAATATCTT
TCTGTTGAACAACAGAAATAAAGGGGATGGGTGAGGAGGATAGTCTTCGG
TGGCCAAGGATATTTGTAGGTACTTTGCAGCACTCAGCAATGAGGAGTGG
GCTTTAGTCCCCCAAGAAGTCTCACAGCCCTGTTGTCTTTACTGTTTCA
TGTCAAATCCAAGACAAGTCAATGATCAGGAAAGACCTTTTTTTTTCTTC
AGTGAAGTTTATTTTCAAGACATTGAACAGTATGATATTTGCTCATTTAT
AAATATTCCCATTTAAATAATCTGAGCTTATATATTTTCACTCTTAATTA
AAGGACTTGATTTAAAGAGAGCACACCAGTCCAAATTGAATTGATCCAT
AGCTATTAATAAAGTAGGCTCTTTTACAGACACTGCTACTTCTTGCCCCCT
TTGAATAAATTAGACCAATGAATAAAACAAACAAATAAATAAATAA
ATAGGGAAGCGGTTGCTCATCAGAAATGTGGGAGCGAATGACAGAGGGTTT
CTTAGAACCAATGTGGCCGTGGTTTCTGTGAGGCGGGCTTTAAGTGAGT
AGGAGAGGTGAGAGAGGCTGGCTCAACAAAAGGGCTGGGGATTGGCCCT
GAAAGGAGAGAGCTGACTGTCTGGCTGATGGACAGGAGATCCTCTTAGC
ACTACCCTAAGGCAGGCAGTTGGGCATTGGTGTAGACAACAGGAAAGTCC
AGGCTATAGCCGTACTCAAAAACCTTTCTGTTCCCTTTCTGCCAGCCCTA
GGGATTGAGTCCACATTCAGCACAGGACTCTCTGGGTACAGCTCTCTTTA
GGAAGACACAAATTGCATGGTGAAGTCAGTTATATCCTGGCCGCTTTGG
TCCCTCCCAGGAAGACGGGCATGTTTTCTGCTTGAGAGGTGCTGATGTAC
CAGTTGGGGAAGTGGGCAGACTCAAATTCAGCTTGTTATTGATTCTAT
CTTGTTGAAGACAAATCGCTTTTCCATCTTCTCTTTGGGTAATTTTTGG
GATCTACACTCTGCAGCGAAAGAGAAAGAAGAATTTTTGTGGGGCAAGGG
ACAAAAATGCTATGGGAAAGATGTTCTTTGGGTGGCCAGAAAGGAACT
GACGAGCAGGTACATGATCAGGAGCCACACTCCTGAGTTGTAAGTGGGC
CCCCAACTTTCTGTGTGATTATTAAGAGCCCTTCTTCTTTTCTAAAAC
TTAGTGCCAAATGCTGAGGAGCATAATGTAGGTGAGAATTTTTTTTTTT
GGGGGGGTGAAATTAAGCTAGAGCTTCTGAAGTACCTAGTTTCCAGGG
GCTTTTTATTGTATTTTCTTATGGTCCTAGAATGACATCAACTTGAA
ATGAAGCTTTTGCTGAGAAAGCTGGAGGTGATAGTGGTGGTGATTTTGGG
AGTGGAGTGGACGTGATAATGGGACCCTTAAGTCATCTATTTCCCAAGG
TGTCTATCAAATGAGAGCAGCCCTAACAAATATATAATCTGTTGGGGTTGT
AACTATGGTAGGACATAATAACATCGGCAAAATGATTTAATTTTCTGCAG

CAGGATTGAAGGTTGCAAGCAGTTAAAAAATTATGTTAAATTTATTTACAT
TAATGCAAAATTTGTCAAATAGACCTGTTCCCAGCTTTTCTAGGGATGGG
GGCGGGGAGAAGGTGGTTGTCTGGGAATAAGTGGTAGCAGGAGGCTGAGA
AGGGCTTCATTCCATAGCATTCACTTACCTCCAGCTGTAGAGTGGGCTTA
TCATCTTTCAACACGCAGGACAGGTACAGATTCTTTTCTTGAGGCCCAA
GGCCACAGGTATTTTGTCTATTACTTTCTTCTCCTTGTAACAAAGGACATGG
AGAACACCACTGAAGAAAGAAGGGGGTCTGTGGTTAGGGACACAGCAGT
GCAGGGTCACCCCAACCCCTAGGCCCATGAGTAGGATACATGTAATTTG
GTAGCCTCTGTGGGAACCCACAGTGAGGTTCTTGGCCTAAGACACAGGA
TAACTTGACTTCTCACAGACAATAGCAGGGTCATTTTGTGATTTAGGGT
TTCCCTCAAAGGCCTGAGGGTTTCTCAGAGCCTCATAGCAGTAGGAACG
GAGAATGAAAGAGGGTCTACATTTTAAATGCTGAAGGAAGGAAGGAAGGA
AGCCATTGTGTCACTGGCTGGCAATGTGCCCATCCACAGGAGCGGAACAA
CTTGATCAATGTGGAAGGAAAGGAAAGAGGTGAGGCTGTACTTCTGCCAG
AAATCAGGCACCAGAACTGTTTCAGGAACAGAGAGTAGCCCATGGGAAGA
AACTGGGAGAGGAGAGGCTGAGCTGGGAAAGTGGCTCCAAAGAGAGACAC
TCATTTTGATCTTCTCAGTCACAGCAGTGTCAATTGGAAGGCCCTGGGA
TCACTCTTACTACCCGATTCCAAAGAAACAGGATTTTCTTGGCCTGGCTG
AGAGCAATAGCTTCCCCCTTGAGTGAGGCTGTCTTCAAAGTCAGCAGC
CTTAGTTGCCACACTCTGTGCAGAGGCTTTGGCTACTGTGGCACGATG
CCAGGCAGATCACACAGCTAATGATGGGTTACCGCACTTGAAACTTTT
GCCCCGTACAGCGGAGAGATATAAGTTCTGTGGGCGGTAAAATTTCCC
TACAAGGAACCACCTGGCATTGGGTGGGACGGATGTTGGGGCAAGGGGGG
AAGACTGGGGAGGGGGATGGACACATTATCGCTCCAGCACTCTTGTTC
GCCTCAACACAGGAAGAGAGAACCCACAGGCAGTTAGGCCATGTCCATC
AAATGACCCCATATTGTGGAAGAATTGACATTGCACTATGCCAAGAGAC
TTGGGTGGACATGGTCTGGGAGTGCTTGAGCCGTCTAATTTCTCAGGGT
CACACTCTGTAAACAAATGCACTGGCCAGTGCAATCAAATGTGCCATTT
CTAGGACCAAAGTTGTATATTCTTTTAAATATTTTTTTTCACTTGTGT
TGATCATTTGCGCTTAAATTAACCTTTCTACTTTGTTTAAACATGGAGAAT
TAGCAAGCTGCCAGGAAGCCAGGCAGGAAACCAGGATGTTTCCATTAC
CTTGTTGCTCCATATCTGTCCCTGGAGGTGGAGAGCTTTCAGTTCATAT
GGACCAGACATACCAAGCTTTTTTGTGTGAGTCCCGGAGCGTGACGTT
CAGTGATCGTACAGGTGCATCGTGACATAAGCCTCGTTATCCCATGTGT
CGAAGAAGATAGGTTCTGAAATGTGGAGCACATGTTGTTAGGTATAAAA
TCAGAAGGGCAGGCCTCGTGAGGCAAGGTGGCAAATTTGATTTCTTGGA
GGACACCTGAGCATATACGGTCAAAGTCTGATGACAACACCAGTAGGGAT
GAAGCTGGGAGTGGGGTGGCTAAGAACACTGGACCTGACACTATTAGACA
TGGGTTCAGCTTCAGGTCTATTACTGCTCACTGTGGCCGAGCAACAGAG
CTACTTAGGTAAAATGGTGATGGTCATAACACTAGCCACAGGGAGGTTA
CGAACCTCTGGTGACAATGTAAGTGAAAGGCCCTGAGAAAGAGTGAGGG
AGTTGCAAATGTCAGTAGCCATCAAGATCTTCTTTAAGAATAGTTTCCAC
TAAAGAGATGATTGCTTTGGTTTCCAGCCTTCTTTGTTTGTCTCCCCGC
TGGGCCTTCTACCTTTAAAGGGCTTTGGCTCTGGGGGAATTGAGTTGGCT
GGGGCTTGATGACTTCCAAGAGGACACAAGTGGAGATCTACTGCCTGCTC
TTGGCTAACTACCTTCTTCAAAGATGAAGGGAAAGAAGGTGCTCAGGTCA
TTCTCCTGGAAGGTCTGTGGGCAGGGAACCAGCATCTTCTCAGCTTGTC
CATGGCCACAACAACTGACGCGGCCTGCCTGAAGCCCTTGCTGTAGTGGT
GGTCGGAGATTCTGTAGCTGGATGCCGCCATCCAGAGGGCAGAGGTCCAGG
TCCTGGAAGGAGCACTGCGGAGAGAGCGAGGGAGGGAGCCTGGTGAGGTG
GTCCTGCCAGGAACCATGCTTTGACATCAGAGAGTAGAAAGCTCAGAGAG
GAGGAAAGGGCTTGAAAGAATCCCGAGCTTCTAAAGATCATCCCTCTCTG
GGCCAGGCGTGGTGGCTCATGCCTGTAATCCCAGCACTTTGGGAAGCCGA
GGTGGATGAATCATTTAGGTGAGGACTTCAAAACCAGCCTGGCCAACATG
GCGAAACCCCTTCTCTACTAAAAATACAAAATTAGCTGGGTGTGGTGGG
GTGCACCTGTAATCTAGCTATTGAGGAGACTGAGGAAGGAGAATCGCTT
GAACTCAGGAGGTGGAGGATGCAGTAAGCCAAGATTGTACCACTGCACTC
CAGCCTGGGCAACAGAGTGAGACTCTGTCTATAAAACAAAACAAAACAA
AACAAAACAAAATAAAATAAAATAAAATAAAAGATTATCCCTCTCTGAA
GCTCAAGGAGGTTAAGGGTGTACTCAAGGGCACACAGCAGGTTAGAGGCA

FIG. 4 (48 of 61)

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GACTCAAGACTAGAATGTTGGGCTTTCTGACACCTTACAGGCTATTCTTTT
AGAATAAATCCCATTTCTACTTTGTTTCATCTTTTTTGTACATGCCCCACC
TACACCATAACATGTATACCTTCTCTATATCTTTTTGTATCCCTAATGCTG
TCACACTATGATTTGCTTTTTTCATGCAGATGACCATAACATTTCCATTCC
ACCTATGCTCACTCAGCAAGTATTCAATTTTTCTACACTGTTCTTTTTTT
TCCTTTTTTCATAACACTGTCTCATAGGCATTCTGCAAATCCTGTGAGAGT
ACTTTTTGTGAAATGTTACCACTTTCTCTTATTTCAGAGAAGCTCCGTAT
TAAGGCTTCACTGAGGTTGCCTTAAGGCATGATAATGGTTCAAAGGCTTG
AAAGACAGTTAAAGAGACCTGTAAGTGCACAAAAGAAAGTTGAGCAGGAG
AGAATTTCTTGCTGGAGCAGAGCCAAAGCTACTGGAAGAGGCAATGGGGG
CAAAGGCCAGGCAGACAAGCCAATGGGCTCCTCCACAGCTGCAGCCAAC
AAGTTATGCCAGTCTTAAACTTCTAAAGAAATATGTTTTTAACAAGATT
GAGGACTGGATTATGAGGCTAGGGGAGGCTATCACAACTGGAATAAAAT
AAAGCCAGAGAAAAGTGGCTGCCTTCCAACCTGCACAACTGACCTAGCTA
GGCTGATGGCTGGGCCACCTAGGAAGGCTACTGAGCATCATATAAAACAG
AAGGGACAGCAGGAATATAACATGGCTCTTTGTAAGGATGAGTCTGAAAA
ATGACCATTTGCTGCCCAAATGCCCTTAGCTACAACCTGAAAATATTTTCAG
AACTGGAGGTTGCAGGATGCTGGAATCTCAGAGATCATCCAGCTCAGCCC
TTTTTTTTTTCAGATGAGGTTCCAAAGCGGGTAAATGACTTGTCAAGGTCA
AACAGCAAGTGAATGGTTTTTCTTCAAGTCTCAATTCATCTTTTGTTTA
TATCATCTATGTCTTGTGTTATAAGCTTCACCCCAGGTAGCAAAAACT
ATTCTACTCAAAAGGGGTAGACATATGTTAGTTCTCAAGATCATCTCTTG
GTTTCAGAGTTTAACTCAAGTGATTGGCATAGGCTGAATCCATCTCTTAA
AAGGATAATCAAATTTATGTTGAAGACTTGGTTGTCTTCTACTATGAAA
TGGGAAACATTATCACTACTCCTCCCTGTCACCACCAAGTGTGGCCACC
ACCACCAACGTTAGTGAGTGACTGTGGTGATATGATGACCAAGTGGCCAG
GTCAGCAAGTGGTGCAGCCTGTGTCTCACTGGAAGAGGTTAAAGTCTTTC
TAAAACAAAATACCATGGCATCAAAGTGGCCAGAACTCCCTTCTTTGAG
CTTTCCTTGTTAGAGCCCTTCTTGGGTTGGGAGTTAAACCCATAGTC
TTACCTTCATCTGTTTAGGGCCATCAGCTTCAAAGAACAAGTCATCCTCA
TTGCCACTGTAATAAAAACAGGGACATGTCTCAATTATGTCTTCTAAACA
GGTTTATTTTTCTTCCCTGTGTACAAGACTTGACTGTTTATAAGAACT
GCAAACAGCCTGCCTCTCAAAGCTGCCTGAAACACCTGGCAAGTTTCACA
GTGATATGCGCAGAACAGTCCAGAAGGCAGATTCTAGGCCTGGCAGGTGG
GCACCTGGGTGCTCCCTGTTGGATCTTGAGGCCTAACCTCTAGCCCAGC
AGAGTCAGCTAAAATCTGAGCTCTCCCTCTCCCTCCAAGCCACACTTTGC
AAAGGGATTCTTGTATTGTGGGCTTGGAACTTTTTCTCCCATTTGCCT
CTGCAGGAAGCCCTTGCAACAACACATCTGGATAGCCTCCAGGTCCCAAG
GCTGGAGGGACTTGTAAATGGGAAGTAGTCTTTAAATCAGATTTACTTGG
CACCTGTTTGGCACTGAAAGAGGCAATTTAGGGGAAAAATCTGCTCTCC
AAGCACAGATAACACTCTACTCTTGAAAGAGGAGACCTGCTCATGTTACT
GGTCTCAGCGTCTCCACTGACCTGTAATAAGCCATCATTTCACTGGCGAG
CTCAGGTACTTCTGCCATGGCTGCTTCAGACACCTGTGTAAAAGGAGAA
AATGAGTGACTTCCCCATGACGGCTACGTTTCATGTGTGATTCTCTCAGC
ATCCAGTGCATGGCAGTCATGCAAAGAAATGATCTCTGAGTAAATGAATG
AATGTGTGAAAGAGAAGTCTTTGGGTCTAGAGAAAAGCATTTGCTAAAC
CAAACCCCACTAGCAATGTATTGGCTAGGAGAGCTGGAGCAGAGGCTTT
GACACTAACCTTTAGGGTGTGAGCTGTTAGATAAGCAGTATCCATTCCCA
GAATATTTCCCGAGTCATAAGCATTATATTACACCTGGCATTTTTGCAAA
AAGCTGAGAGAGGGAGGCAGAGAGGGAAGGAGAGGGAGAGACAGAGAAAG
AAAGAGAGAGAGAGAGAGAATATGCATACACACAAAGAGGCAGAGAGACA
GAGAGACTCCCTTAGCACCTAGTTGTAAGGAAGATTAAAGTCATACTTGA
GCAATGAAGATTGGCTGAAGAGAATCCCAGAGCAGCCTGTTGTGCCTTGT
GCCTCGAAGAGGTTTGGTATCTGCCAGTTTCTCCCTCGCTGTTTTATAG
CTTTCAAAGCAGAAAGTAGGAGGCTGAGAAATTTCTCTGTTGAATACCTG
ATTTTACAATCAAGTTAAAGGAAAGGGGAAAAGAGTATTGGTGGAAAGCTT
CTTAGGGGAGGGGACTAATAAACTGAGATAATTCTCTGGTTCATGGAAGG
GCAAGGATGAGCAAACTATGACACATTTTGCAAATGTATCACCATGCAAA
TATGCATTGTTTTCTGACAATCGTTGTGCAGTTGATGTCCACATTAAAA
TACTGGATTTTCCACGTTAGAAGAATGTTTAAATTTAGTATATGTGGGA

FIG. 4 (49 of 61)

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CAAAGTGGGAAGACACACACAGATTATATACA.GCACATACACTTTTCTTCATTCA
 CTTCTTTTGACTTAAGTTTAGGAATCTTCCCACTTACAGATGGATAAATG
 GGTACAATGAAGGGCCAATAGCCCTCCCTGCTGTATTGAGGGTGTGGGT
 CTCTACCTTGGGTGCTGTTCTCTGCCTCGGGAGCTCTCTGTCAATTGCAG
 GAGCCTCTGAGGAGAAAATTGACCTTTCTTGGCTGGGGCAGAGAACATAC
 GGTATGCAGGGTTCAGGCTCCTGACGGAGTTGGGGCAACCCTGGAGATAA
 GCTCACACAACCTGCAAGACCAGGTGCTGTTACCCTAGCCAATCTCATG
 GATGAACCAGCATCAATGCCAGATGAGCTCTGCCTAAAATGATTTTTTGGT
 GAACCTTGAAAAGTGAATATTGTTTTCTGTAAGAATATCCATCTGAGACT
 CTATCTCTTGGTAATACCAAGAGTTATCAGTTTCTCTTTAACCGAGACAC
 CAGCAAAGTGCCTGCTCCAGGGTACTGCCAGGGGAGCCCTCCATTTTGTA
 GAATGAATGAGAGTCCAGGTTATGAACAGTGCCTGGAGTGTAGGAACACC
 CTCCTTTGCCTCTTTGACAGGTCTGCATCATAACACTTTTTTTTTTTTTTT
 TGAGACAGAGTCTCACTCTGTGCCCCAGGCTGGAGTGCAGTGGCACGATC
 TCGGCCCCCTGCAAGTTCGCGCTCCCGGGTTACACCATTCTCTGCCTC
 AGCCTCCCCAGCAGCTGGGACTACAGGCACCTGCCGCCACGGCCGGCTAA
 TTTTTTGTATTTTTAGTAGAGACAGGGTTTCACCATGTTAGCCAGGATGG
 TCTCGATCTCTGACCTTGTGATCTGCCCCGCTCGGCCTCCCAAAGTGTT
 GGGATTACAGGCGTGAGCCACCGTGTCCAGCCTGTAACACTTCTTATAGC
 ACTGAGTTGAAACCTTGCTCCTCCTGTTCTCTCCAGGAACTGAAATCTT
 TTTGAGCCAAGTCTAGCACAGTGCCTGGCATGTACATTCAAGGTGTAGAG
 TTTGCTGCTTGAATGGGTGAATGGGAATTTGACAGCATTTTTATTCAAAT
 TAGTATGTGCCAGGTATCGTGCTCGCTCTGCATTATCCAAGGGAGTGAGC
 CTCTGTGCAAGTATTTGAGACACGAGGGAAATAGGTTCTACTGTGGGAAA
 AAGAGCATTTCATGGACTTGCTCTCCAAGCAGCCTTCTGATTTTAAATT
 GGCTCCCAGTATCTTGATATCAGGAGTCAGTCACAAGAACTCCATCTTTA
 GTAAGTTATATTTTCCACAGGAAATCTAAAAGCTGTTCAACATGTTAGTT
 TCCTGTGAATTTGATAAGCCATAATCCATTCTTAACACTGAGCCCTCCTG
 AAATTTGGTGTCTGGTCTCTGCAGATAGCTAAAAGCCCTGTCTGGGTGGCC
 TAGGGGACTCCTCTGTTTTTGCCTCCACAGGATCCACTTGCAAATTAACC
 ACTGGTTCTCCCGTTGTAGGAACTGCCACCTTCTCTCAGAGCCTGTCTTTC
 TTCCTTCCCTCCTTCCCTCCTTCTTTCTTTTCTTTCTCTCTCTCTTTCTT
 TCTTTTCTTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTT
 TCTTTCTTTCTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTT
 TTTCTTTCTCTCTCCCTCCCTCCCTCTCTCTTTTCTTTCTTTTCTTTCTTTC
 TTTTCTTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTTCTTCTT
 TTTGCTCTCTCCCTCCCTTCTCTCTCTTTTCTTTTCTCTCTCTCTCTCTCT
 CCTAGACAGGATCTACCTTTATCCCCAGGCTGGAGTGCAGTGGTACAAT
 CATGCATTCAATTGCATGATCACAGCAGCCTCAAACCCCTCTCAGAGTCT
 TTATGCGGCAACCAGCAGGGTCTGGAGGGTGGTGGCTCTGTGAACCTCTC
 CTGACAGAACACAGAGATGTCTTTGGTCTGTTGATGTGATTACAAGCTGA
 ACGAAGGAGGATCAAAGCCAGTGACAGGAAGGGAGATATGCAAGGGACCC
 GAGCATCAGCTCTGAGTTAGTCCATTCTGCTTCTGGGACTTGGGATACAG
 GTCAGAAACCTTGAGCTTCTACTTCTCCATCTTCCAATTGTAGCATCCAG
 GACCTCAGAATCTGCCAGCTAAGAGGAGCCGTAATGATTGTCTGGTGGGA
 TATGGTGGGACCACAGAGATGAAGACATGAATAGCTATTTGAATGTGAAC
 AGCAGACGCAAGAAATCAAGGCTAGGAGGGTGGAGTGACTCATCCAATAG
 CACAGTGTGGTTGAAGCAGCCTAGTATCCAGTTGCACTGACGCCCTGAT
 GCTTTGCTCTGAGGGGAAATTTGGAGCCATGGGGCAATGCCCCCTGACGT
 AACAGTCTCCACAGTTCCTGCCATGTCTCATCTTGGCCCTGTAACCTGGAC
 CCAAATCTGCTACCATCCCATCCATCTCAGGAAGTGAAACCTCTTATGTC
 AAATAGGTTGTGCAACGTATGTATCAGATCCTGTCTTCCAAGGAGACCG
 CTCAGGCCACAGCACTTCCCTCCGATCCCCAATGAGCAGAAAATATCTCG
 CTATAAACATAGTTGGCACTAAGGGAGGGAGTGGAAGAGTGATGATGATG
 TAGATGGTGATGTAGCCCCAAGGAAGTGGAAACAAGCAGAGATGGGGAGCT
 GGAAATGCCAGGATGCTCCAGCTTTTGGGGAAATTATTCAGCTCTTGAGTC
 ACTAAAGCCTTTCTCAGCTGCAAGTTCTCTTTTACCCTGTCAAGTCATT
 TTCCAAGACAGGAGACTGACATTTATTCAAAGCAGCAAGTGCCCTGATAC
 CATCTTGTGTCTAATCATGGGCTTCGACGCCAGTTATCAAGGTTGATCTC
 ATCTCATTGGTCTTCAATCATTTTGAACAAGAAGACAAGCAAAATAATCA

FIG. 4 (50 of 61)

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TGGGTTAGTTCCTTATATTATTGTGTGTACATGCAGTGATGTCTGTTCTTT
GTAGTGAGCTGTTCTTCTTGTTCACCTCTTGCTTAGAACAGAACTAA
GCAATCTGCCCCAACATTTTCCCCAATTTCCCATCTCATTCTTGGCACT
GGCTTCCTAATATTTGTTCTTATGAGTCATTTTCTTGTATCATTTCCATG
AGTCCCTCTGGGATCTTAAAGTATGAAAAATGTTGTGTGTACCCACACCT
GTCTTTGTGGATATTTCTCTCCTTTCCCTTCTGCTTCTGGGATTATTTGG
GAATGGGCACTATGATTTTATCATATCGCTTCCACTTCCTTTATGGCAT
CATCTCCAATGGGCTTCTTCTCCCTCTTGGATCCAGGTTCTCAGATTGGG
GACATGCAGAGTCCAAGGAACATTCCATTCTCCTCCCTGGTCTAGAACAA
GGAGGGCTTAGATATATGAGCAGGTGGCTGGGGCTGGCGAGCTATGTAGT
CTCCAATGGCTTTTCCCTGATGTCGGAGTTGTTATGTCAGTTCTGGGAGA
CCAATAAGACCTTGTCTTCTTGGATCCATCAGAAAAAGCCCCCTGGGT
GGGTAAGATGGATGGCAGGGCTCTCCTACTCTATGTCTTTTCTCACACCT
AGTGGGTATAAGAGAGGGGACCACAAACAGAGGGGGCTCTGGTACCACTT
ATCCAGGGTCTGGAAACATTTTCTGTAAAGGGCCAGATAATAAATGTTTC
AGGTACAACCTACTCAACCTTGCATCATTTTCAAGAAAGCAGTCAGATAATA
CATAAATGAATGGGTGTGGCTGGACTTGTCTGCGGTCCCCTGTCTTATA
TCATTGTATTATATCATTTTTTCTTACATACAAATTTAGAAGCAATACTT
AAAAAAGCCGTCCTTTATTGAGCACCTACTAAGTGCCAGGTACCT
TTTTTCCCTCATTATCTTAACTCTTATAATAACCTTTAAAGTAGA
TAATATTGAACCATTTGACCTATGCAGAACTGAGGTTGAGACAATAAAT
TATTTAAGACCGCACAAACAGTAAATGCTGGAACCTACGACTCAAATATGG
GTAACTGAACCAAAACAGATCTTTATTTCTCACTTTTAATTGTTACAT
ATGTTTATTGCCTCATCTCCTGTCCACATGGTGCCCATCGGCAGACTCCT
TTCTCATCTCTCAGTGATTGAGTGACATTCTAACTACATTGGCCTGGCAG
ATTCACCTCTGTCCCTTAAATGTTTCCACATTGTCTTTTAGGATTGAGA
TCCTCTCTGTTCCCTTGTCTTCCCTCCTTTCTTCTTCTGGCGGTGACGTG
CTGTGTGAATTTGTTTCTTCTCCTCTCAGGGTAGTACTGGGACTTTCCA
AATCAGGGTTTTTAATGATCTCTCTTCTTCTTCTGAATTTCTTCTTAT
TCCCATCTACTTTCTCATCTATAAGTGGCANCTTTGTTGCTGGAAGATAT
CCCTTGTGCAGGGATTNCTCTTTAANAATTTGTCNNNACC

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GTGATCGTCAACCTCCCACCCTGTAGGGCCTCAAGCATTGAGGACAATCA
CTGGCTGCCCATTAACCCAGAAATGTTGCCGAGACAGGAGGCGGTGGCCC
AAGTTCCTGGAATGGGGTATTATTATGTCAGCACAAAGGCCTTTGCACAA
ATGAAGGCTTTAAAAATGCAGTCCTAGTCAGGTGGAGGAGGGCTTATAGG
ATTCCCAGGAATCTGGATCATTCTCTTGAGAGCTTCCCTTGTCTCTGTT
AAAACCTCACATCGTACGGCCCAATAACAACAAAAATGGATGTAAATTC
TTGAAATAACTTGTGGATGGGGGAACAAGGCCACCCCCCAGATCTGCCA
GAAGCTTCAGGTGAGGGTCCCAAATGCCAAAAAGTCTGGTATCAGAGAGG
ATGGCCAGTGACNTGGGGACACATGCCCTTTGCTGTGTCACTCAAGGAGC
AGCAGCTTCGGCCCCGCACAGTGACCAGGACCCTGGCTTCCCACGCTGGG
CAGGAGCTGGTGTCTGATGAAGGGAATGCCTGGCAGCACGTGTCTGTCTGT
CTCCTCGTGTGAGCTTACCTGGCTTTGCTGCGAAGAGGCCACTTGCATTT
CTTTATTTTTTATATTTTTTTAATTTTTTTAAATTTTTTATTTTATTTTA
TTTTTATTTATTTATTTATTTTAAATTTTTTTTAAATTTTTTAAATTATG
CTTTAAGTTTTAGGGTACATGTGCACATTGTGCAGGTTAGTTACATACGC
ATACATGCGCCATGCTGGTGCGCTGCACCCACTAATCGTCATCTAGCAT
TAGGTATATCTCCAGGTTAATCCCTCCCCCTCCCCCACCACCAAC
AGTCCCCAGAATGTGATGTTCCCTTCCCTGTGTCCATGTGATCTCATTTGA
ATTTCTTTAAAGGTGGAATCTCTCAGTGGGGTCTAATCTGTTTCAGAAATA
TCAAAAGAGTATCCTTGGGAATGACTGGAATTCAGAGTCATCTGGTAAT
CCTCATAAAACAACCTCTGGATGTCTCTCAGCACATCTCCACCTTGAAC
GCAGGAGGCTGGTTCAAATGGAGGAGCATCGCTCTACTGCACTTTTTTTT
TTTTTTGGCCATAAGTGCAAAAGGGGATACGTTTCATGTAAATAAATCAA
CTGCAAATCGCTAGTTATGCTGAGCCCTGTCCCGTGTGTGGACACAAAG
GAACCAAAGGCTTTTCTCCCGCCCAACACACACATAACACACACACAAA
ATCATAAAAAACATACATACCCCAACATAACAACACACACACACACA
CAAAATATATACACACACACACACACAAACATGCCACAAACCTGTGTCC
AAAAATAAATCTACTGGTGGGTTTGTGGTCTCCCTAACTTCAAAAATGA

AGCCGTGGACCTTCGCACTGAGTGTACAGCTCTTAAAGATGGCATGGAT
CCAAAGAGTGAGCAGTAGCAACGTTTACTGTGAAGAGCAAAAGGACAAAG
CTTCCACAACCCAGAAGGGGACCCAGCAGGGTTGCTGTTGGGGTGGCC
AGCTTTTACTTCCTTTTGGCCCCCTCCCATGTTCTGTTTCCATCCTATCAG
AGTGCCCTTTTTTCAATCCTCCTGTGATTGGCTACTTTTAGAATCCTGC
TGATTGGTGCATTTTACAGAGTGCTGATTGGTGCCTTTTACAATCCCTT
GTAAGACAGAAAAGTTCCTGATTGGTGTGTTTTACAATCCTCTTGTAAGA
CAGAAAAGTTCCTCAAGTCCCACTGGACCCAGGAAGTCCACCTGGCCTC
ACCTTTCAACTCCATAATGGCATGAAAATACATATGTTGTACAAAACATA
CATACACAAAGTATACATGCATCTCCCCAAATATACACATACCACAGAAA
CATACACACAGGAAGTACGCTACCTGTCAAAGTCTGCATGGTATTGCC
TCTGCAGTGAGTAGTTAGAAAAGTGAATTTGTTTTTCAATAAATTGGAGT
CCTTAAAAATCGTTGTAGATAGAAAATTTTTAAAAGTATATAAAATAAA
ATATGTATGTCCTTTGGTCTAGCATTACACATGTAGGAATTTATCCTAG
TGGAGTAATCAATGATATATGCAAAGATTTGGACAAGCATATTAAGCACA
GAATTATGTATGCATATGTGTGTATATATATATATATCTGATACATAT
AATAATGTAAAAGTGAAAATAACTCAGATGTTCAAAATTGAGGATTAGTT
AGACTATGATCTGTCCATATGTGACATACAAGTTAGCTGCCCTTATTCT
CTCGAGCTTCAACCTCCTATAAACAGTGTCCCTTGTATATCAGTATTGGT
ACAGATAATCGAAGTTATTGAGGTTTTACATGGGGCAATAAAGGCAAGAG
TTTATGAATACTCCATACTACACTAGGTAGCACCCCTATTAAAGACAAA
CTCTTCTCTCTCATTTCCCTTCCCTTCCGGAACCACTTGGTTGAATCTCT
ACAAGTCTCTATTGCAACTGCCTCAACATGGCACCTCCCTGCATCTCCA
TCTTCCCTGTCTGAGAGCAATGGCCTGCTGCCCCCACTCACATCCTC
ATTCAATCCAGAAGTGAGCACACAGAAGTGCCTACAGTTACCCCAACCA
CCTTCTTAGAAGATAAGTTAGTGTGTTTTGACTTTTTAAATTTTAC
TTCTCTTTTCCCTTCAATCTCATCCCATCCCAAGAGGTTTATCAAGAA
GTTCTCTAAAGATATGTGTCTCCTTATGGAATTTAACAGAAATCAGGGAT
TTGTATTCTAGCCATCAAGGGAATAACATTTTCCAGGTCTTTAGACAAA
TAATGGAATACTCTGCAGTAATTAGATACACTATTGTAGAAAAGTATTGA
TGAAATGGAACGATGTTTGAGATATCATATTGAGTAGAAAAGGCAAGATA
CATTAAAGTAGGAAATGTATCTTACAAAATAATTTGTGACACACACTCCTA
TATTTGTATGTTATATAAATGCGTATGTGAAGAAAGGCTAGAGGATGAGA
CCACAGTCTTCGGTGAAGTTAAGAGATGAGGCTGCAGCATGCTCAGAAA
GGCCTGGGTTATAGTTCTTCCAGTAATTAAGGATGTGATCTTGGGTAAAT
TGTCCATCCTCTCTAACTGCACCACCTTTTGTCTGTAAAACAGGAAGGA
TGGTATTTACCCCCAGGGTCATCAAAGGATTTGGTTGGAGAAAAATAAAT
AAATGGGCTGAGCCCAGACCTGGCACAGTGAGAGCACAGTGGTTGACTAT
TGTGCTGGCCTGTTGTTTCTGTGTTATTGACATGCTGCTGGTGGTGGTCC
AGAAGCTATTACCTTAATTGGTTATGTGGATTCCCTCATACTGAGCAG
CTGTGTGTGGTGTGTAACATAGCCATACACAGTAACTGACAAGGGCA
AATGTGATGGAAAATGCAAGGAAGTGCAGATAAATAGCTAATGGGCTGT
AGAAGGAAGCTAGTCTTGGAGGGCTTGATCAAGGAAGGTCTTTTGCAT
GTCACCTTTGAAGAAGAGGGGACATAGAAGAGGTATAGTGCATCCCGGAG
TGTACCTGGAAGGGAACATGAAAAGAGGACATTTTTCTCTGGGACATGGG
GACTCCACTTGCATGAACTCTGGAATTGGGGCAAAGAACCATCATGAGAA
CAAGGGCTTCTTGAACCTCCAGGCTCATTGGCTGATCTAAACCCTGTG
TCCCCTCTTTCCTTCACTCTCCTCTGTTTTCTATACCTGTATTATTGGAC
TGGACTGGAAGCCACCTGATCTATCACAAGTACCTTGAAATGTGTTGAAT
AGGTGTGGCACAGTCTTAGCAGAGTGGCACTACCCCAACAGGAATTTGT
TTATACCTTTGGCATGGAAAATAGCAGGAATGAGTGATCACTGATAACT
GAGGATGCTATTTATTATTGGCCAAAGGAATACTTGTGTTGTATTGTCAT
AACCCTCACAACCTGTTGATTACAAATGAGTACCAGACCTAGCTCCTTC
AAGTAAAGGATCCTGAGAACTGAAGGCAAACAGAGCTCCAGGAGTCCAAG
ACAGAGCCACAGACCACGAGGATCCCTGGCCCAGGTAGGTGGTCTCCTG
CACTGGCTTTCAAGGCCAACAGGATGGATGGGGAAGTAGAGTAGCATCTG
GCCATCTAGACCCTTGCTTTTTATCCCCACTGGAAGCACATCTGAATTC
TAAATATGATCTCTGAGACCTGCCCAGAACACCTTGCTCTCAGCCCCAGT
AGCAGCCTGCTCTCTCCAGGAGGGCTTCCACTAACAAGTAGGGCATTGC
TGGAGGGCCAGGCAGACACTAGCTTAGGAAATCCACCAACCCTGGAAATG

FIG. 4 (52 of 61)

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CTAGTCCCTTCTCTGAAGGCTCAGAAGACTGACTTTAGAGTCTAGAAAAAT
ATTGGTCCTTGGGAACAGATTTTGAGTGCAAAGAGATGGACTTCAGATGG
CCAGATGCACTGCTTCTTTAGGGAATTCTGTGAAAGCTCCCTGCATTTAT
CTTAATACAGGCAGCAGATTTTATGAGTACCCCCGAGGGATGGCCCCAGG
TCCTCCAGCCTGTGAGCATCCTTCTGTCTTCAGCAGCACCACAGTATCT
TTATATGTCTTTGGATACCTACGTTTCTGCCAGACATCTCTTGCTCTGAT
GTTCTGGCTGCCAAATTCTCTGTCAAGCGCCTCCAATTTTTTGTGTCTT
TGATTTACCCCAACATGACAAAGGCAGTTGTGCTTCATGTATTCAGGGAT
ACTGCCAAACCACAAACAGGTTAAAAATCAAATAGCAGATATCCCTGTTCC
TAAAGACCCATCAGCTCTACCCACCTGCTCCTGCTCACCGTCCTTATTGT
TGAGTCCTGAAGCCCTTCTTGTCAATTTTTATTTTTTGTCATGAACAATTT
AGTTCCCTTTGTCTCACTCCTAAACCTTTCTCAAAGGATTGGATTTGTAC
ACAAACTGCCTATCTCTGCAATCTTAGAAGTGATATGATTCTGAACAAAT
CACTTAACTTTTGATTTTTTATTGGTAAGATGGGAATACCAATTTTTGCT
CCACTTCTGTCTATGTTGGCCTGGGCTGATGTTGAAAGCTCTCGGTCAA
CTGAGATAGGGTGTGAGAAATTTATATATATAAATATATCTCTCCAACC
CCTCCCAATGAAGCAAGTCACGTGAGTCAATCCTACCCTAAGATATTAGG
GATTGAGCCTCCTGGGACATTTGGTGGCTTAGGTTTTCATGAAAAGAGGT
TGCAGAGCAACTGCTTTTTGTTAGGCAAAGATTAGGCTACTGCAGAGACT
CAGCAAGACTTCTATAGAAGGTGTGAGATGGTAAGTATTTTAGGCTTTGCT
TGCCAGATCTCTCAACTAGTTAACCATGCTATTGTAGCCTCGAAGCA
GCCAGAGACAATATGTAAACAAGAGCATGGCTGTGTTCAATAAACTTT
ATTTAAAAAACAGTCAGGGACCGGATTTGGCCAAAGCCATAGTGTGCC
AGCCCCAAGACTAGAGCAATGCACTTTTAACTTTTTTATTTTTATTTTGT
AAAATGCCAAGATCCACAAAAATGCTATTGCACCCCGTGTGTTAGCACTG
TGACTCAAGGTTTGGGAAATTCTGCTTTGAAGGCGTGATAGACAGGAGAG
CATGGTCTGGCCCCCTTGGTGCCTTTCTGGTTGCAGCGAGCATTTCAAAC
ACAGAGCAAGGCCAGTGGTCTGTTGAGCACTAGAGACATGCAGCAAGGTG
TCCTGGGGTGAGAAGATGCCATAACTGGTCCCTTTCTATCTCCTTAGGT
CTTGGAGTTCATTCATTTTCTGTTGAGTAATAAACTCAACGTTGAAAAT
GTCCTTTGTGGGGGAGAACTCAGGAGTGAAAATGGGCTCTGAGGACTGGG
AAAAAGATGAACCCCAAGTGTCTGCTTAGAAGGTAAGGTTCTTGTAAGAAATC
TACCTCAGGGCCAAAGTGTAATTCCTAGAGCAGAACTTTGCTAGGTGCTG
TGCACAGACCCAGTTGTTTCTGCTGACTTGCACAGTAAGTGAGCTTTCA
AATTTCCCTGGACAAATAACTAGACAAGAGAAATCTGGAAGAGAAAAGG
AAGCTTTGCTTCAGTGTCCAGGCACATCAGGTAGTAGATAAAAGGATCGT
CCTCACCTACAGATTTGGGGCTTTAGCATCCTGTTTGCCAACTGGATGGT
TGCATATGCTTCAAATGCACCTCTTCCCTCCCAACATTCCCAAGTGGAA
GAGAAGCCTCCGATGAGAAGGAACTCTCTAAGGCTGGGCTGAACAAATGA
CCAGGCACAGGGCATCTGAGTATTCATGAGGAACACATTTGGGTGTTG
CCCATGGGGGCAATAGGAGGAGGCTTTTGACCCAAATGATTGTCTACTG
AGGTGTGACGGGAGAGGCTGTGACATGCCAGAGGCCAAACCCGTGATCC
AGTTCATCTCTATTCTATGTTTCTGAAGAGGGAAGCTATGATTTAATGTC
ATTACTATCATGCTGCTCTAGTATTTCTCAGCACATACACAGAAGAGGGA
ATTAAATGGTCCTTGATACCCCTAAATCCTTGGAAAATCCGAATTGCATA
TGCTAACCTCACTGCGTCTGACTGCAGACCCGGCTGTAAGCCCCCTGGAA
CCAGGCCCAAGCCTCCCCGCCATGAATTTTGTTACACAAGTAAGGCCTC
GGGGTGAGGTGATGGGGGTGGCTGAGGTGCGAGGGTGGGGATGGGGGATG
GAGCCATTGGGTCTCTTACAGGGTGAGAGAATTGTAGAATGGGGACACC
TAAGGGTGCTGGATGGGGCTGAAGTCTTTCTTTGTGGAAGCAAATCCCA
TTAGGAGATAACTCTGGGAAAGATGAGCCCCGGGAGGGGCAGGTGATGCT
CACCTGCTAAGAGGCAAGGGCAAGGAAGAGTTTGTGCTGGGAACCTTC
CAGGTGCCTCTTCTGACCATAGCCAAGAGACTGGAGACACAGACCTCCTC
CCAGCACTGAGGACAAACAGCCATGGGGCCAGTGGGGGTGCAGGGACACC
CACACCACTAAGGGCTCAGGGCGGCGCTTCAGAGCCTGAACCTTCCTCT
CATGCTGCCATTTGAACACCACAACCCCTAATAGGAACTGTAAACATT
GCCACTGTTGAGGTGTGGAACCGAGACAGACAGTGGAGATTCCCTGCCC
TAGGTGACACAGGTAATAAGTGACAGATGTGGAAATTTAAAGGTACTATA
ACGTCTCTCTGCTGACTCAGGCTTAAGGCTCCCATCACCTCCTCTCTC
AGGACAGAGTCAGGAGGCCTCAGCCTGAGCCCCAGCTCTAGTGCAGGTTT

FIG. 4 (53 of 61)

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ATGTGGAATACTGAGCCTCACTAGTACAAATGGCAGAGAGGACCAAATGG
 GACCAGGTGTGTAAGGGTGCCTGGCACAGTTGGGGGAGGCTGCTGTGCT
 TCTCCACCGCTGCTGCTGCAGTTACCTTTGATGTTTTAGTTTTGTTGTAG
 TTACACCATTTGCTGGCTTTGGATCTGCACTGTGTCCACTCCAGGTGGAAC
 CACGCACACAAGCCTCTCTGTGGGCTGTCTGACTTCTCCTTGTGAGG
 GCTGGGATCTCCTTCAAATCTGGCGGAAGTGGTTCTCCAAGTCTGGTCTT
 CAAACGTCAGCAGCATCAGCGCCTAGAAGTGTAGGAATACACATTCCCA
 GGCCCCACCACAGACCTCCTGCCTCAGAACTCAGGGCGCTGAGGCTCTA
 GGGGCTGCTTTAAACAAGCCTTCCAGGTTATCGTGACGCACCTTGAAAGTC
 TGAGAGCTACTGCCCTACAGAAAGTTACTAGTGCCCTAAAGCTGGCGCTG
 GCACTGATGTTACTGCTGCTGTTGGAGTACAACCTTCCCTATAGAAAACAA
 CTGCCAGCACCTTAAGACCACTCACACCTTCAGAGTGGCCTTGAGAAAGA
 TTTGGGGTCAAGGATCATGAGCGAGAACACCACTTAAGAGGATAGTGAAC
 TAGTCTGCATGTGAGACGCTGAGATCCTATGTGAGGCTGTGATAGGAGGG
 AAACAGAAACCAAAGGAAAGAACAGCTTTAAGAAGCGCTTAAGAGGTACA
 AAGTAAATGATGGTGCTAGAAAAGTAGCTTCTTAAAAAGAGCATTTTCC
 AGTCTCACCTGGACTAACTGAATGAGAATCTCAGGAGTGTGAGGCCAG
 GTATCCATGGTCTTAAATGCCACCCACCAGGTGATTCCCAGTGTGCACC
 AGGGGTGAGAGTCACAGCCTTAGGCCATGCCACTCAAAGGGTGTCTTCAG
 ACCAGCAGCAGCCACAGCTCTGGGAGTGCATCAGAAAGACAGAGGCTTGG
 CACCACCCACACCTACTGAACCATAGTTTGCAGGTGATTTCTTGCACATT
 AAAGTGTGGGAAATGGAAAAGCTTAGAGTTTCACTAGCTCGGTGACTCTC
 AGTCAACCTGCACCTGCTCCATGAACTCAGACTGCCTGGGATGGGCCAG
 AAAAGTCTCTGAGGAGATTCTGATGTAAGGCAGGGCTGATAACCATGGAT
 CTCATCTGACCCCATATCACTGGGGAGTTACTTAGGATCTTGCCTGGGGC
 CAGTCATCTCTTCCATAGACACTGAGAGTGTCCACGATGCTTGGGGCACT
 ACAGGGTGGGAGGTGGAGGATCACGGGTGAGTCAGATAGGAAGCCTGCTC
 CTGGGGAGCTTACAGTGCTATAGGGCAGCAAGCCAAGGATGCCAATACCT
 GTGTGCAGGTACCACTGACGAGTGCAGAGCGCTGCAGCACCAGAGAGGAA
 GCTACCCTGTGCAGAGGGGGCTGAGGAGGGCTGCAGGGAGATGACAGGAA
 AGCCGGTGTTACAGGAGGAGTCCTCCCCACTCTTGGGCATGAGGAGACC
 AGGAGGACATTCTACAGTGAGAAACCCAGGCAGAGGCCATGTGCTTATGG
 CATGGGAAAAGAATGACACCTTAGACTTATTCTCTACATTAGAATTGCCT
 ACCACAGATACCCATATTATAGCTTCACATAGTGTGGTGGTTACTGTGTT
 TTCATATTGTACATTTGCCATTTTCCAGCCACCCACCCATTCTTGACAG
 TCACTGGCCAGCCTGGGGGGCCCTGTTCTTTATCAAACAAGTGCTGAG
 CTCTTTGCAGAGGTGAGGGTCACCTGTCCAATCAGAGGCCAGGAGGGAAC
 GTTCCCTTTTAAAGACCCTACTCTAGGCAGGCCTGGCCCAAATGAGTTGCT
 AGGAGCCACGCCCTAAGAACCCTCTGAGCACTGTTGTGGCTGGTCCTGC
 TGCTAGAAGTTGTTCTCCAGGGCCAGGTGCAAGATTTGTGGCTTTTCAA
 AGGAGCCACTAAAGCTCCAGCTCAGCCTTGACGGTGCTGGGCTCCTGGG
 GGCTTCTGCTCCAACCCTCCCAACTCTTCCATCACCGCTCCCTTAGCC
 TGGCCAGTGCAGGGATCTGTTCCACTCTAGGCAGTGTGAGGGAATGATG
 CCTCCAGTCAGAGGGTGCAAAAAGAGAGTTAAGAAAAACAATGATTATA
 AAAAGTCTTTTATACGCCAGACATTTTCTTTGCTCAGGCTAAGTGCTA
 CTTATTTAGTAAGCATTTTAGTTCTCATAACTCCTCTCTCAAGTAGGTG
 CTGCTATTACTTTTCAATTTACAGATGAGGACATTGAGGTTTGGAGAGACT
 TAGTAACTTGTCTCTGTCTTACAGCAGAGCTGGGATTTGAATCTATCTG
 TCCAAATCTGGAACCCATTTGCTTGCACAGAAAGCTTAATTGCTTGTCCC
 AGCAAGATAGAAAGCCTGGGAGTGGAAGAAATATTCAGTGGCTGTGATGT
 CTGAGCCACAGGCAGGGTGGAGAGCTAGGGCTGGGGCCCTTGGACGTGG
 GGAAGAAAGGGCTGAGTCTTCCATTTTCAATGTGAAGTGTGATATCTGG
 TGATATTGATCTAGGTCAAAGGTGAAGAACTTAACCCGAAGAAATTCA
 GCATTCATGACCAGGATCAAAAGTACTGGTCTTGGACTCTGGGAATCTC
 ATAGCAGTTCCAGATAAAAACTACATACGCCAGGTGACTCTCAGTTTTG
 GCTGTGTTTTCTGCTCCACCTAGCAGGGGTAAAGCCCTCTGCTAGGTGG
 GCTCAACTCCATGCTATACCATGCCCCATCTCCAGCAGGTGGTGAAGCG
 AGGAGGAGAGGGCCAGGGACTAGGGCATCAGATGAAGGGTCTCTAGCAA
 TGACCAGATCTGAAAGTAGTCTTTCTGGAAGGGCTGGAGAAAAAGAAGGA
 GGCAGACACTTAGACTGGAAGAAGAGGAGGCTTAAACCGGTGTGATGGAG

FIG. 4 (54 f 61)

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GGAGAAGTGGACCACAGAATCAAGGGAGAGGGACTGTGCATCAGGCCTGA
AACCCACAGCAGACAGGAGAGACCTTTCCCTGCTCTCAGAACCACACATG
TTCTGACTGTCTTTTCCAGAGATCTTCTTGCATTAGCCTCATCCTTGA
GCTCAGCCTCTGCGGAGAAAGGAAGTCCGATTCTCCTGGGGGTCTCTAAA
GGGGAGTTTTGTCTCTACTGTGACAAGGATAAAGGACAAAGTCATCCATC
CCTTCAGCTGAAGGTGAGAGTTCTAGCTCAGTTTCTGCGCCTTTGGGCTA
CQCCAAAGTAAAAGGCCAAGATCCTCAATGCCTCTCGCTTTCTGCAAAT
TCTTATCTTGGCCAATATAACAGGGACATCCACCTTTCTGGAAGCACCAG
GCAGAAGAGCCCCATAACTTCTTCTCTGGTTCCTTGCCCCCTTCTAGGGAA
GGAGGAGAGACTCCTCACAGCGGGGAGACAGCAAGGAGCTGAGCACCTGT
TCTCCTCTCCTGGGCTCACTGGTCTGCGCCTGGGCGGGTGGCGGTCCCC
TCCTGCTGTGGCCCTCCATGTGGCAAGCAACACAATTGGGCCAGGACCCT
GGCGTGCTGCTGTAGGGTAGGAGGGTGTGAGGGAGCACTCGGAGGGCAGT
GTGTCTGCCCTGCAAATTTAGTCTGGATGGAGCATCCTTTCACTTGAGG
GGAGAAATCTTAGGAAGCTGAATTAGATACAGATCTAAGCCATATTCTCT
AATTTTAAAACTATAGAGCTGAGATTTTGGTATCCATCTGACTCTTACG
TCTCTCTCTCTCTCTCTCTCTCAGTTTATTTTAAATCTGGGGGACA
AGAAGGCCTGGAAAAGAGGGCATGATTGCTTATCATCCCTTAAATACCAG
TACCAAGGCTGACACGTCATCTTTCCCAAGGACCATCTGCCTTCTCTCTT
TTCTCTCTCTCTCTGTAAAGGCCTGGAGGATGAGCACATGTGCTGTGTT
TTCTCTCTCTCAAAGCCTGTGCTATCTAATTAATCCCTTTTACCTCACA
GAAGGAGAACTGATGAAGCTGGCTGCCCCAAAAGGAATCAGCACGCCGGC
CCTTCATCTTTTATAGGGCTCAGGTGGGCTCCTGGAACATGCTGGAGTCG
GCGGCTCACCCCGGATGGTTCATCTGCACCTCCTGCAATTGTAATGAGCC
TGTTGGGGTGACAGATAAATTTGAGAACAGGAAACACATTGAATTTTCAT
TTCAACCAGTTTGCAAAGCTGAAATGAGCCCCAGTGAGGTCAGCGATTAG
GAAACTGCCCCATTGAACGCCTTCTCTGCTAATTTGAACTAATTGTATAA
AAACACCAAACCTGCTCACTAACTTTCTGTCTATTGGGTTTCAATTTCTCA
TTTCAGCTTTAAGGATTTGTGTTTTTAGGATATAGCAAGAAGCTTGTTTA
ATTACAAAGTTCTGGGTTGGAAAGAGACCGGCTTCTGCTTGTGTACTGCT
ACCCTGAACCATCAGACATGCATGTGTGTGTCATATGCTATGATGTGGCC
AGTCTGAGTGCAATACTTGCAGCGGGAAGGAGCAGCTGGGTGCATGCTGT
GCTCTAGAATTAGTCTTCTCTACTGGGGTTTGGTAGATTCTGAGGGCATT
GATCCTGGGGCAGAAGTGGCTGAGTCTGTGTCTAGGGTACAGTGTGCAAG
AAAGAAATGTAACAGCAAGTCACAATCCAGCCAAGTGATAGTGGAAGG
GGTAGTTAGGTCCAGATAAGGAGCAGGGTGACTTGACCTGTGGGAAAGG
CACAGAGACAAGGAATCTGGGTGAGATGACAGCCAGGAGACCAGGTGAGG
GAGGAGCCAGGTACTGTCTGGGAGGCTTGTCAACAAGGGCATGGTCTTAT
CACTAAGCAGGGCTCAGATCCTCATAATGGGGGAGTGGAAGGCTGGCCGA
ACAGAAATCAGGGCCTGGAAACAGAGTGAGGGGTGGAGACAGGAGACTG
AGGCTTGGAAATTAGTTTATTAGTTTTAGCTCTTCAGTTACAAGCAATAA
TAATAGCTTCTAGCTTATTTAAGCAACAAGTATACTACAAAAGGAGCTTT
CTAGAAGGATATTGGGTATATTCAATTTCTTACTGCTGCTGTAACAAATTA
CCACCAACTTAGTGGTTTAAACAATGCAATGTATTATCTTGCAGTTATGG
AGGTCAGTCTGGAATGTGTCTCACTGGGCCAAAATCAAAGTATCAGCAGG
ATAGCATTGCTTTGGGAGGCTCTAGGGGAGAGTCAATTTCTTGCCTTTT
CCAGCTTCCAGAGGCCACCTGCATTCTTGGCTAGTGGCCCACTCCCATC
TTCGCTGCTTGGGTTTTTCTCACACTGCTTTGCTCTGACCCTCCTGCCTT
CCTCTTTCACATATAAGAAGCCTTGCAATTTACATCGGGCTCACGTCAAT
ATCCAGGATACTCTCCCGTCTCAAAGAGGCTTAACTTTAAATCACAGATGC
AAAGTCCCTTTTGTATGTCTGTGTAACATATACACAGGGTCTGGGGATTA
GAATGTGGACATTTTTCGGGGTGCCATTATTCTGCCTATCATGTGAAGTAA
CTTTCAAATGGAAAGACATGCTGAAGAAAAAGTCAGGGATTTCTGGCAG
GCCAGAAATGACAGAAGGCAGAAAACGTTGGTCCCATCACTCAGATGGGT
AAGAGCCAATCATGCTTTTGTGCTAGTCAAAAAGATTGAGATTCCAAGC
AAAGCATGCAACTGCCCTAGTTTGGGTGCTGTGCTGACTCCTTGGTCAGT
GAAGGGCAGCACACCTTGATCAATACTCCCTCCAAGACTGTATCCAACGA
GGCCAGTGATGTTCTCAAAGCAGAGCTAGAGAGCTAATCCAGGAGAGA
GGCGTGTTGGTGGTGGGAGGAGCAAGCTCAGCCGTAAAGGAGTAGT
AGGGACAGCACCTTAGGCATGGAGGCTCAAGTGAGATGATACCCATGGGA

FIG. 4 (55 f 61)

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AAAGCTCTGATAAGGTCAGCTCCTTCTGTTTCTGATCCTGATGGTGATG
TGATCAACACCAGCCAGTGACAAAAAGTACATAGTATATTTAGTAGAT
GTTTCCACACAGAGAAATGGTAAATATTCAAGGCGAGGAATACTCCAAA
CATCCTACCTTGATCATTACACATTCCGTGCATGTAATGAGTACTTGCA
GTATGCCATAAATATGTGAAATATTATGTATCACTATATAAAAGAAAAA
AAATGTGGCCAGGTGACATCCATATTTTGGAGAGGAAGGCATGTCTTCT
CATATATCACAAAATATTTTACAAACAAAGACACAGCTGTTCAAATTA
GTCTCTGAGCCGGGGCTGTCTCATGGCAGTGAGGACTCTGGTTCCCTTAC
AGACTAGCAGAAAGGAGATGGGGCTTACTGACCATGGCCTTGAGGAGGCT
GAACATGCAGGCCAAATGGAGACACAGACAGCCTGGGCTTGGTCCTGCTC
CATCCCCCTTCCAACCTGATGAGATATAGTGAGTCACTATGACGTGGGTCA
CTCATGCTTCCTGTGAGGCTCCACCAAGACAGCAAGTGCATCAACACCTT
ACGGAAGCACAAAGGCCCTGTTTGTGTGTGACTTCATGAAAGGCATGGTTG
TGGTGATCGCATTGAGTAGGCTTTTGGGTGAGAGGTGAAAAACCCCACT
ATCATGCATTGCAGCCCTCTGGTGGAACTGTGCTTCAGGCTCTAAATTT
CAGGCTCTAGACTGACTCCAGGATGAGTATTTGGAAGCTGAAGTCAATCT
GTGGTCTCTTCTCCTGTAGAGCAGGAGTCAGCACTTTTCATAGAGTGCCA
GATTCTATATATCCTGCCACATGCTCTGTTGTTACAGAACAAGAAGGCC
ATAGCAGCATGGCTGTGTTGGCAAATACACAAAACAGGCAATAAGCTGT
ATTTGGCCTTTAGGCTGCAGTTTGCCAACCCCTGCACTAACACAGAGCTT
AAAGGTGGTGGTGGTGTGCTGGAGCTAGCTTATATCAGCTTGCAATAGCC
AATTGCTAACATCTCTTCCAACTCTGTGTCTGTGCCTTGATGTTGATAG
TTTGAAATTGGCTACCCCATTTAATGCTGCAATCTTTTCTCACCCAGCA
CTACTGACTCCCCCTTGCCCTGTCTTATTTTTCTCACTCTAACATGCTGT
ATAGTTTTCTTCTTACATTTATTGTTTGTGTCTTCCACTAGCATGTATGT
CCCAAGTTCTTTGCTCTGTGATGTATCCCAAGAACCCACTGCAGTGCT
TGGCACTTGTAGGAACTCCATAAGATTTTTATAAATGAAGAAAGGAAGAA
AAAAGAGAGGGGAAAAAGGAAAGGAAGCCTTCTATTTAAATGATGGC
CTTCTCCATATTTCTATAGTAATATGACTTCCCTTGCAAAGGGGGATGCA
TTTTGGAAAATGTGTATAAATAAACTCAGGTGGTTTGAATTTTCAATTTT
CTAACTGTAATTGTAATCATTGGTCTTTATGTTTAGTGAAAAAGTTTTGG
CCCTTATGCCTCACACCTGAGAATCCCAAAGTATTGGTTTGTAGAGCTC
CCATAGAGAACCATAAACTGGGTGGCTTAAAAACAAGAAATGTATCGTC
TCCTGGTTTCCAGGAGGCCAAAGTCTGAACTCCAGGTGTTGGTTCAATCTGA
GAGCTCTGAGAGAGAATCTGTTCCAGGCTTCCCTTCAGTTTGTGGTAGCT
CCAGGGTTCTTGGCTGGTGGCAGCAAACTCCAGTCTCTGCCCCCATCT
TCACATGACTGTCTTCTCTGTGTTTCTGTGTCCAGATTGTCTTATAAG
GACAGAGTCATACTGAATTAGGGCTCACTCGAATGACTTCATCTTAAGTT
GAATCTATCTGTAAAGACCTTATTCCAAGTAAGGTCACATTCACAGCT
ACTGGGGGATAGGACCTCAACATATCTTTTTGGGGGACATAATTCAACTC
ATAATACCCAACATGATAACTGTTTCATCCCATGAAATTTAATGTCTCTCA
AAAGGTGATCTCAGGGCATTTAATCTGTGACAGAACTCCCATAGGAAAC
ATTCCAACAGAAAGCTCCTTTCACAGCTGGTCACTCCTCCTACCCCATCC
GAGGTCTTGGGGCAGGGTGAGGCAGGTGGGGACAAGAAGAAGGCTGTCTC
GGGTGTAGAAAGAGAAGACCCTTATTCACCCGGCACTCTGTTCAATGAATG
AGCTATCCAGCATAGGATATAATAAATCGCTTTAGGAGTGGTAGACTCCA
AACATTTTTTTGGTCCCAGTTATCCTAATCAATTAACAACTCTAGAAC
CCATCTTGAAGTGCAGGCATTGGGACATTATGAACTTACACAGAATTCA
AAAATTTACAAGGGCTAAATAAAACAGGGTCTGACATCTAATATTTTCTT
CCCACATTTCCATGCACTGTCTGGCTCAACCATCCCCAACCCCTCACTCTC
ATCCTGGTGGACACATGCCTAGTGATGTGATCAGCTGGTTACAGGGGGC
TGGTGATGGTGGATATACAGCTTTTGCCAATTTCCATGGCATAACTACTC
CAAATATGGCCAATTTCAAACATCAAGGCACAGACACAGAGTT
TGGAAGAGATGTTAGCAATTGGCTATTGCAAGCTGATATAAGCTAGCTCC
AGCACAGCACCACCGCTACCTTTAAGCTCCTTGTGTTAGTGCAAGGGTTG
GCAAACCTGCAGCCTAAAGGCCAAATACAGCTTACTGCCTGTTTGTGTAT
TTGCCAACACAGCCATGCTGTCTATGGCCTTCTTTGTTCTGTAACAACAG
AGCATGTGGCAGGATATATAGAATCTGGCAGTCTTTAATAAGTGCTGACT
CCTGCTCTACAGGAGAACACAGATTGTCTTCAGCTTCCAAACATTCATCT
CTGAGTCAGTCTAGAGCCTGAAATTTAGACTGAAGCACAGTTTCCACCAG

FIG. 4 (56 f 61)

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AGGGCTGCAATGCATGAAGTTGGGGTTTTACCTCTCACCCTAAAAGCCT
ACTCAATTTTTTACTGCAAAAACATGTTATCATCATTATTTTTTACTTAG
CCCACCTTTCTTGGCAATTTTCCATAGGAAAATGCATTCTAAATTTCAA
CTAATCAGGGGACTTGGAGCCTCTGGACACCCCTTGTTCCTTGCCACA
GTCCCTTGCGAAGGTGCCTTATCAGAGCGGCTCCATGCAGGGGCTCAGG
ACAGGATCAGATGTCAGTTGCACCAAGGGGGCAGGGACAGATCCTCTCTG
CTEACCATGCAGAAGGGACTGTTCAAGTGCACCGTCATGGTCCTGGTGATT
TCTGGTCCATAAGGGAATTTTACATGCATCGGGTGATTGTCACATCAGC
ACAACACTGTGAGGAAGGCAGAGTGAGAATTTGTGTGCCCATTTTATAGG
TGAGAAAACAGATGCAGAGACATTAAGTAACCTTACCACAGTCATGCGGG
TTTTAAGTGGCAGACTTTTCAAGTGTGTGACTCCTAGTCCAGAGTCTTT
GCACTGCCCCCTGAGGTGCTAAAACCTCTACTGTGCTTAAAGACTCACTTGG
GGAGCTTCTTAAAAAGAGAGATTGCACAACCTGAGATTCTTGTTTAACTG
TTTTGGGATGTAGCTCAGGGATCTAGCTGCCTTAAAAAATAAACTCCCA
AGTAATTCTGATGCAAGCGGTTCTTTTTTGTCCACCTTTGAAGAAACACT
GCCTCCTCCCCATACATTTTATTAGAAAATGGTAACATGTTTTTCAGCCT
GAGAGCCATTTCTGGGTGACCGGACGTCGGCAGCCCGCTGTACTAGCTTT
CAGTCTAGGCTTAAACACACATGATAGGAGATGTCCTACTCCAGATGATA
TGAGTCTGAACCATGGAAAAATTCATTGTGTGGCACATCTGGTGGGTGT
GCACTGTCCCCAGCAGTGAGGCACCCAGTGAAGACAGCAGCTGGGAGAGG
CTTAGTTACATGTCAGTGGGACAGTGTGGGCTAGACTGCTGAGCCCTCTGC
AGTTTACTCTGTGTGTCAGGCAATGAGGGTGAAAGGCTGATCAGACCCACGT
GCAGACCATAACCTCCAGGGAGACAGATATCAGTCAGGACAACCCCAAGT
GTAGCTGGAGAAGCAGTGCCAGGTATGACCGGATGTGTATCCAACCAGG
AAATCTGCATATAAATATAAGAGGAGAAAATGAACAGATGTTGCTCTTAT
ATGTAGATATTTATGAAGAGCATATAATTTTGTGTGTGTTTAAGAA
GTTTATAAGTATGCCTTAAAAATGTATAGTATATACTGTAGGTATTTTTT
CCATTAGATATTTTGTGTCTTACTTATCCACATTGACATTGTAGCAAC
AGTATAATATAACAACCTCCTCTACAAAAGCAGAAGGAAGTGAAGCTTTG
GAAGGAAGCACCAGTGAGCTTGCCCCCTTTCAGGTGGGTGCAGTGAGCAG
GAGTCAGTGAGGTTGAGATCCTTTGAGAGGAGGCAATCATTAAACCAGGAA
ATCTGCACTGACCTCCTGGCCACACCTAACCTTGGACAATGGTGCTTGA
GCGCCTTCCAGCTCTTAAGGCTTGCGATTTCTTCTCTCACTCTTCACCC
ACGATGATTAAATCTTCTCTACAGAGTTGGACAATAAAGCCTTGAGTTC
CTGCCTCCCCTGGTGTGATCACGAGGCATAGACATGGCCAGGAACATGTA
GGTGTCTTTGAAAGCTGAACAAGTTAGTAAATTTCAAACCTCATTTACC
CACCAGTAAATGGGAATAATAAATACCTATTTTACATAGGGTTGACAA
GAGGAGTAAAGAGGGATTCAATGAAAGTTCGTTATTATCATTGTAGTAG
CAGTGTGATAATATCAACTGAAAGTTCATTATCATTATTAGTAGCAGTA
TTGATACACCTCTTTTCTGTGCCTTCTCACTGGTGGGCCCAGGCCATCAG
CAATGCCAGGGTGTGTCATGGATCTCTGCTGCATCGGGCACCAGCTGTGTC
AATGGTGAGAACAGTACAAGGGTGGGCAGGGCAAGGCAGGAAGCACCAG
GAGCAGCAGCTTCATGGGGTGAAGATGTCAGGAGCTTAGGGACAGTCAGA
GCGGGTGTGCCCTCTTGTGGAGCCTTTCTGCGTGGGTAGGAACTGCTG
CAGCTGTGGCCATGGATTACCTGAATATGGGTGGAATTAGGCATTACAGC
TGGGTTAGCTGTGCCTAGAAGGAGGAACTCTAAACTGAGAACTTGTCCCT
ATTGCCACCTCTGATAGGCAGATGATCCATCCATCAGTGGCTGAGCTGAG
GTGTGCATGGGGATGGGTAAGAGCCCACACACAGGGCTGATGACTGAGTC
TATTTAGAACAATAGATGTAAATCTGATAATGTAAATGTGATAGATTA
TTTTGTCAATTAGAAATGGTACCATATAATTATATATACATAAACATG
TATACATATACACACATATACATGTGTGTATAAACACACACAGTATTGTC
CCCTACTCATTCCATAAACCTGATGCCTTTAGCTGGGATTCCCAGCTTTC
ACTCTCCTCTCTGTCTGCTGTCTATATCCTCCCCATCCTGTAATTCT
GGCTTATATGCCACTTCTCCTAAAGCCCTCCTCAATCCCTTGCTGGA
AGTGACATTTTCTCTTTGAGCTGCCCTGCTTGTGCTTTGGTGAGGTCA
GCTGTATTGCAGTACCTTGTATTGTGGTTGTACATCATCGTATAGAATT
AATTTCTGACACATTCCGTATTTTCAAAGGGCCTAGTGTGGGGCTTTAA
CAGTAACTACGCCACCACGCCAGTTAATTTTTTGTATTTTTTGGTGGAGA
CAAGGTTTACCATGTTGGCCGGGCTGGTTTTCGAACTCCTGACTTCAGGT
GATCTGTCTGCCTCAGCCTCCTGGAGTGCTAGGATTGCAGGCATGAGCCA

FIG. 4 (57 of 61)

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CTGCACCCAGCCACCTATCAAAATTTTAAGTGCCATTTTTATTATTTTATT
TTTTGTAGAAATGGACAAGCTGATCGCAAAATTCACATGGAATTGCAGGA
GGTTCCAAATAGCCAAAACAAATCTTGAAAAAGAAACAAAGTTGGAGGA
TTTACACTTTCCAGTTTCAAGACTTAGCTCTTAGCTACAAAGCTACAGTA
ATCAGAACACTATGGTCCTGGCATAAGTGATGCTGGACAGGTGAGCCCCA
AAGTGGGACTTAACCTGTGAAGGTTCTTGGCCTTGCCAGGAAGGAATTC
AAGGGCAAGCCAATGGGACAAGAAAACAGCTTTATTGAAGGGGCAGTATT
ACAGCTCCAGCCCTGTTACAGCTCCAGCCCTGTTACAACTCTGACTACTC
CTGCACAGAAGGGCTACCCTGTAGGCAGAGAGTAGCAACTCAGGGCAGTT
TTGCAGTCATTTATATCCACTTTTAAACACATGCAGATTAAGGGACAATTT
ATGCAGAAATTTCTACGGAATTGGTAATAACTTTTGGGTGATGGAGTCAT
CATGGAAGGGGGGGCGGGGAAGTCCCTGGTGTGCCATGATGACGGTAAAC
TGATATGGCGAACTGGTGGGTATGTACATGAAAAGCTCCTTCCACCCCA
GCCCTGTTTCAATTAGTCCTCGGTTTGGTCCAGTGTCCAAGTCTGCGCTC
CAGAGTCAAGTCCCACCCCTACCTCTTAAGGAGAGATGTAAATACATGG
AATAGAATTGAGAGTCCAGAAATAATCTCATACATCTATGATCAATTGAT
TTTCAGCAAAGGTGCCAAGACCATTCAATGAGGGAAAGAATCATATTTT
TTCAACAAATGGTGCTGGATAACCCACATGTGAAAGAATGCAACTGGGGCC
TTATCTCACACCATATACAGAAATTAACCTCAAAATGGCTCAAACACTTAC
ATGTAAGAGCTAAACTATAATATTCTTAGAAGAAAACAGGGATATATCT
TTATGACCTTGGATTTGCTGGCTGATTCTTAAATGACACTGAAAGCACA
GCAACAAAAGAAAAAAAATAGGTAAATTGGACCTCATCAAAATTTAAAA
CTTTTATGCTGGGTGCACACCTGTAATCCCAGCACTTTGGGAGGCTGAGG
CAGGAGGATCTCTTGAGCCCAAGAAGCTGAGGCTACAGTGAGCCGAAAT
GTGCCACTGCATCCAGCCTGGGTGACAGAGCAAGACCCTGTCTCGAATA
AATAAATAAACAATAATATAATTATAGATCTCTGGATCTTGCCTTCGGAG
ACTGACTCACTAACTGGTCTGGGTGGGAGCCAGCCATTTGTATTTTT
GAAAACCTCTCAAATGATTTTACTGTGCAGCCAAGGTTGAGAATCACTGT
ATCATAGGGTTGGACTCCTAACTGGAAACAGTTTGCACCATCAGGTGTCTG
CAGCATCTGATAATAGTTAAGCTTTCTCCTAGATTTTCTGATATTAGA
TGAGTCATGTTTACAAGTTTTTACCAAGAGACAACTATCTTTCTGCCCT
TACTTTCTCTCTTATACTATTCTAATCCCAGAACCCCTTTGGAACCTCCAC
TGAGAGATGAATCTAGAAAGTGACTCTCTTGGCTACAACAGAGAGTAATG
TTGGCCTGTTTGTGCCAGATCCAGTTGGTGCTGGTGGTGGGACAGCACCT
CCCTGAAATCCCCTCCTCTCCCGTCAGATTCAGTCCCCCATTTGCATCAC
GTACAATCATCACTATGGGTTTCTATTACCTTGCTAGGGCATTGGAGGT
ACCATATATACCAACTATTAGTTTTTGGCCATGGTTCCCAAAGTGTGGAC
TGTAGGGCACCTCAGCACACTCACGAGGTGTCATGGGATATTTAAATATT
CTGAAGAAAACACAGTGACATCTGTGAGGCCCCGTGAAAACCGTTGGCATT
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GCTCACATCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGCAGATCAC
GAGGTGAGGAGTTGAGACCAGCCTGACCAACATAGTGAAACCCCGTCTC
TACTAAAAATATAAAATTAGCCATGCATGGTGGCATGCACCTGTAACCC
CAGCTACTCAGGAGGCTGAGGCAGGAGAATTGCTTGAACCTGGGAAGCGG
AGGTTGTAGTGAGCCAAAATCGTGCCACTGCACTCCAGCTTGGGTGATAG
TGAGACTACATCTCAAAAAAAAAAAAAATGAGAGAGAGAGAGAGAAGCAGA
ACCATCAGGTGTTTTCTTTTGGCTTAAAGTACTCTGTGAAGAAATTCCTGG
GACACGAAGGATACCATGAAGTGAAGATTTTGGGAACCTCTGCTTTAGA
AGCTGGAGGTAGCATTCCTTGGGCACAGTACTGCCTTGGGATCAGCAAAT
CCTTTTGATGGTGCATTTAGGTGTGGCAAGACAGCTCTTAGAGTGGGACC
GGGATGTGCTTGGAGACAGAGGGAAGTATGAGCTGCCCCGATAAAGAC
ATGCCAGCCTGAGCAGAGTGTAGTGACTCATGTCTGTAATCCTAGTGCTTT
GGGAGGCTGAAGTGGGAGGATTGCTTGAAGCCAGGGGTTTGAAGATCAGCC
TGGGAAACAACAAGACCTCTACAAAAAAAAAAAAAGAAAAAAAAAATTAACCA
CATGTGGTGGCATGCACCTGTAGTCCCAGCTACCTGGCAGGCTGAGGTAG
GAGGATCACTTGAAGCCAGGAAGGTAAGGATACATTGAGCCATGACTGTG
CCACTGCACTCTAGCCTGGGTGACAGAAAGAGACTCTGTCTCAGAAATAA
ATTAAATAAATAAATAAATATATAGTGGCCATGACATCCCTAGAAAGACA
AGGTCCTGGGAATAGGTAGAAGCCAAGGGAAATGAGAAATGAGAGGGGGC
CCTGGAGCTGGAAGTGGGGGAGCAGGATGGCCTCTGAGAAGTTCTTGATA

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TTGGTGTCACTGATGTGTCTGATGTTTAGTTGTAATTATTATTGCTGGGCC
CTGTCAATCCCTCATATCTGATAGCTCTTTGCTAGTCAAAGTGTGGTCTGG
GGATCAGCGGCATCAGCATCACTTGAGAACTTGTTAGAGATGCAGAACTCT
AGAGCCCCACCCGGGACCCAGAAACAGAGCCTGCATTTTAAACAAGCTCCC
CAGGTGATTCTCACACACTCGCATTTGAGAAGCACTGGGCTAGTTGAC
AGATTCTCAGGCATGGCTGACATTGAAATATCCAGGGAGCAGGCTTGGCA
TTAGGATGTTTTAAAGTCTTCCAGGTGTTTCTAAAGCCAGGTTTGAGGAA
TTACTGGGCTGATACAAATGCTTTGTGATGATGCTTTGTGTGTGTGTGTG
TG
TGGGTCACTTGGCACCAACACAGGAAACAATGGAAATATGTGAGCAATG
CAGAAAGGTCAGGAGATAAAAGAAATTAGTGACATGAGAGGTAATCCTC
GGTGTTAGGAAAGAGGGTAGAGCAAACCAGGTTTTCCACCATATGTTGGA
TAGGGGGTCAAGTAAATTTCTACTTAAAAATTACAAACAGGGGCTGGGCG
CGGTGGCTCATGCCTGTAATCCCGCACTTTGGGAGGCTGAGGAGGGCGGA
TCACAAGGTCAAGAGATTGAGACCATCCTGGCCAACACGGTGAAACCCTG
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TTGGCATTAATCTCTATCAAAACAAAGATAGTCCAAAGCAATGGGTTCCAA
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CAGCCCTTGAATAGAGGAGCAAAATGATACACAGTGGTAGCCCTACCAAT
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GCTGATAGTCTGAGGCCATGAAAAGTCCACCTGCAGTAGTGGTAGGAGGA
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TGGTCCCGTGGAAGCCTCACACATGGTACACAAAGGCTGTCTTGAAAAGA
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TTTCAACAGTTGTCAAATCCCCTACCCAAAATGAGAATTTTAAACAGAAG
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CATAACCACACGAATGGAAGTGGCCACCCAGGAATCAAGACAACGGTCAC
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TTAAGGTGAAAAAGCATGAATGTTAACTTCTTAAAAAGGTACAGCATC
CAATTCAAATATTTTTGTCCTGATTTTAATGCTAGTTGATGTAGTGCTAT
TAAAATTTTGTTCACATGGACACAGAGAGGGGAACAACACATAACAGGG
CCTGTTGCGGGGTGGGGATGAGGGGAGGGAACTTAGAGGACAGGTGAACA
GGTGCAGCAGATCACCATGGCCACATATACCTATTTAACAAACCTGCAC

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GTTCTGCACACGTATCCCATTTCTTTTTTTTTTTAAGAAATAGAAAAAA
AATAAAATTTTGTTCACTGATTCTTCCATTTTAAAACTTGTTTGCATGTG
GTTTAGGATGCCCTTACTTCAGCAAAGGAGAAGGAATAGGAGGGCCTTAG
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ATTTTACATGAATGACACAAGTATTCTGAATAAAAAAATAATTGAACATT
GTTAAGAACAAGGTGTCATGTAATTTATTTTTCATAAATAAAAAAATTAT
AGTGGCTTAGACTGAAAGGAACAGAGAATTTAAAAAATTAAAAAGAAGCC
TTAGTATATTTTTGTATATAGTTTCCATGTGCCATATTTGCCATAATTGG
ATGAGAATTTTTTGACCTCTGGCAGGGTGACCCTATATTTTCANTNTATA
AAGCGTGCATCATACC

MVLKCIIPPGDSQCAPGVVRVTALGHATQRVSSDQQIIPQI.WECIRKTEAWIIIPILL.NIISI.QPGGPCSI.SNKCI.SSI.QRSASA
EKGSPILL.GVSKGEFCI.YCDKDKGQSIIPSI.QI.KEKI.MKI.AAQKESARRPFIFYRAQVGSWNMI.ESAAIIPGWFICTSCNCN
I:PVGIXNXVIDFII.GKAQKRGTGSE

FIG. 5

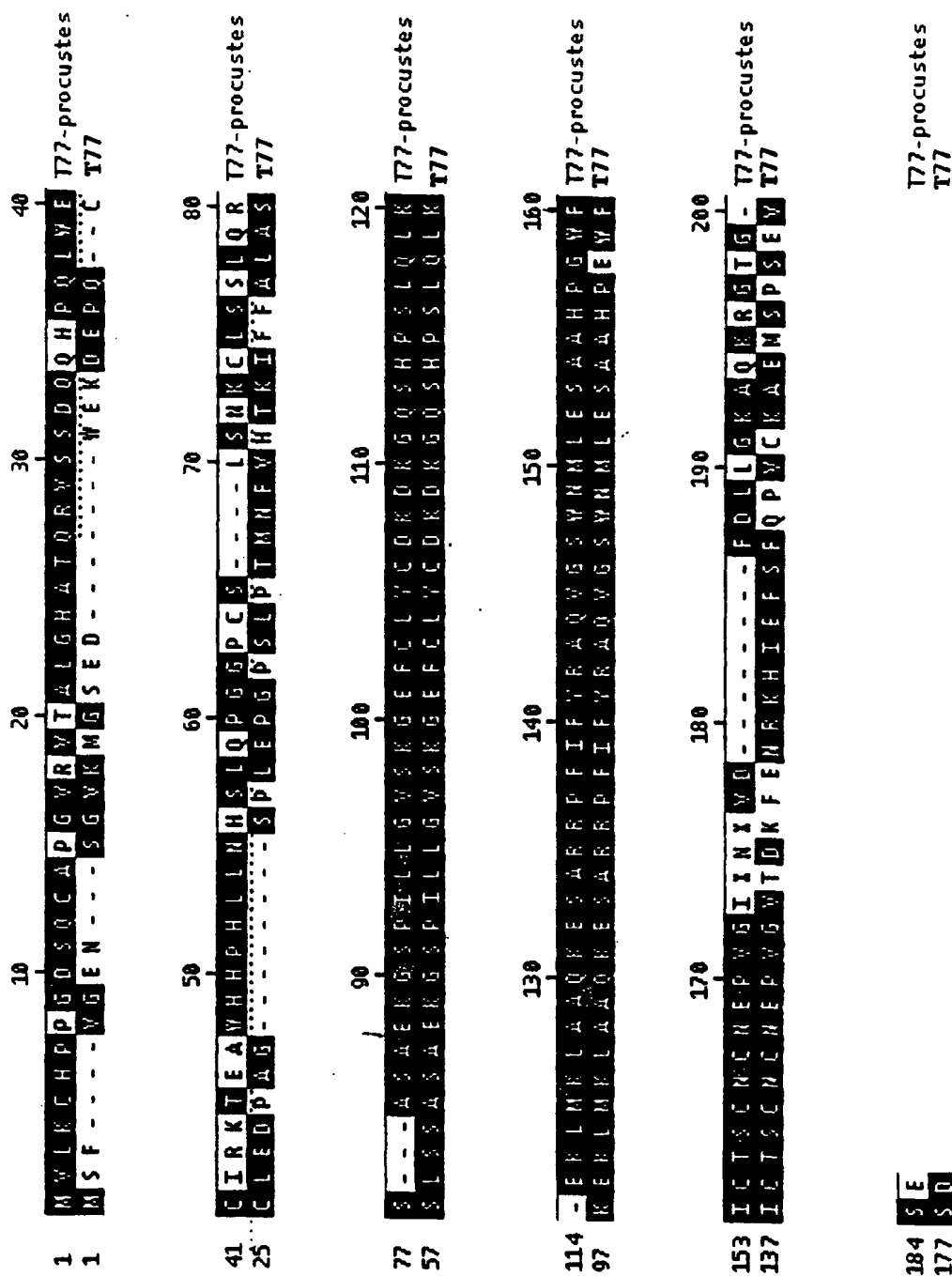


FIG. 6



FIG. 7

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/16102**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(6) : C07H 21/02, 21/04, 1/00, 14/00, 17/00; C12Q 1/68; G01N 33/53

US CL : 536/23.1; 530/350, 387.1; 435/6, 7.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1; 530/350, 387.1; 435/6, 7.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

DIALOG: MEDLINE, USPATFUL, WPI, BIOSIS. Search terms include author, "TANGO" and protein

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	Database Medline on Dialog, US National Library of Medicine, (Bethesda, MD, USA) AN 09370320. SONNENFELD et al. 'The Drosophila tango gene encodes a bHLH-PAS protein that is orthologous to mammalian Arnt and controls CNS midline and tracheal development'. Development. November 1997, volume 124, number 22, pages 4571-82, Abstract.	1-22



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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"B" earlier document published on or after the international filing date	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"A" document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

21 OCTOBER 1998

Date of mailing of the international search report

30 OCT 1998

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